PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PLGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY

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DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PLGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY**" submitted towards partial fulfillment of the requirements for the award of **MD in OBSTETRICS & GYNAECOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Ashima Taneja**, Professor & Head, Department of Obstetrics & Gynaecology, **Dr. Navjot Kaur Bajwa**, Professor, Department of Biochemistry and **Dr. Kanupriya Jain**, Associate Professor, Department of Obstetrics & Gynaecology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

To

my Teachers

&

Family

LIST OF ABBREVIATIONS

cffDNA	Cell Free Fetal DNA
CVS	Chorionic Villous Sampling
DBP	Diastolic Blood Pressure
EOPE	Early Onset Preeclampsia
FGR	Fetal Growth Restriction
LOPE	Late Onset Preeclampsia
MAP	Mean Arterial Pressure
NIPT	Non Invasive Prenatal Testing
PAPP-A	Pregnancy Associated Plasma Protein - A
PE	Preeclampsia
PlGF	Placental Growth Factor
SBP	Systolic Blood Pressure
UAD	Uterine Artery Doppler
Ut Artery PI	Uterine Artery Pulsatility Index
UtA-PI	Uterine Artery Pulsatility Index
β hCG	Beta Human Chorionic Gonadotropin

ABSTRACT

Introduction: First trimester biochemical screening is a non-invasive method of prenatal testing done at 11-13^{+6} weeks for detection of aneuploidy. Preeclampsia which occurs in 2-8% of all pregnancies is a significant cause of maternal morbidity and mortality and fetal complications. First trimester biochemical screening with PAPP-A, free β-hCG combined with PlGF and uterine artery doppler can help in early prediction of preeclampsia and aneuploidy.

Aim of study: To study the predictive value of first trimester screening combined with PlGF and uterine artery doppler for preeclampsia and aneuploidy.

Materials and methods: All pregnant women at or between 11-13^{+6} weeks period of gestation attending the outpatient clinic or admitted between 1st March 2021 to 31st March 2022 were included in this study. A total of 90 women with singleton pregnancies were recruited. Maternal serum levels of β hCG, PAPP-A and PlGF were analyzed by specific immunoassay. Nuchal translucency scan was combined with uterine artery doppler for pulsatility index. Mean arterial pressure was noted. Patients were divided into preeclampsia and no preeclampsia group based on the development of preeclampsia after 20 weeks. Both groups were compared based on demographic parameters, risk factors, biochemistry of serum markers. Correlation with obstetrical and neonatal outcome and performance of MAP, PlGF and UtA-PI for preeclampsia was done. The patients were divided into low risk and high-risk groups on the basis of first trimester biochemical screening for aneuploidy. Comparison was done for performance of PlGF for aneuploidy.

Results: The cutoff of UtA-PI was >1.82, the cutoff of PlGF was <32.95 pg/ml and the cutoff of MAP was >115 mmHg for preeclampsia. The combination of mean UtA-PI, PlGF and mean arterial pressure done with the first trimester screening had a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 100%, 76%, 37.93%, 100% and 79.07% respectively for prediction of preeclampsia at 95% confidence intervals. The cutoff of PlGF for aneuploidy was found to be 56pg/ml. The combination of first trimester biochemical screening with PlGF for aneuploidy had a detection rate of 85.88% as compared to 77.89 % with β hCG and PAPP-A alone.

Conclusions: Adding mean UtA-PI and placental growth factor to the routine nuchal translucency scan and first trimester biochemical screening (β hCG, PAPP-A) from 11weeks to 13^{+6} weeks can improve the detection rates for preeclampsia as well as aneuploidy simultaneously. This combination strategy will be cost effective and also it will allow a timely intervention to prevent adverse outcomes.

Keywords: First trimester screening, aneuploidy, preeclampsia.

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INTRODUCTION

Preeclampsia occurs in 5-7% of all pregnancies and is a significant cause of maternal morbidity and mortality especially in developing countries. It also increases the risk of Fetal Growth Restriction (FGR), low birth weight, preterm birth and perinatal death.[1-4] In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women.[5]

The Maternal Mortality Ratio in low-income countries in 2017 was 462 per 1000,00 live births versus 11 per 100,000 live births in high-income countries.[6] Preeclampsia and eclampsia together are the second most common cause of maternal mortality worldwide.[6] Globally, preeclampsia and eclampsia account for 10–15 % of maternal deaths. Preeclampsia is responsible for over 70 000 maternal deaths and 500 000 fetal deaths worldwide every year.[4]

Preeclampsia has serious maternal effects which can be life threatening such as placental abruption, acute renal failure, cerebral hemorrhage, hepatic failure, pulmonary edema, disseminated intravascular coagulation and progression to eclampsia.[5][7]

Preeclampsia can lead to fetal complications like fetal growth restriction and oligohydramnios. Perinatal death is primarily related to premature delivery, placental abruption, and intrauterine asphyxia. Neonatal complications such as necrotizing enterocolitis, respiratory distress syndrome, and intraventricular hemorrhage among women with preeclampsia are not uncommon.[7]

Developed countries have reduced the incidence of eclampsia and associated mortality through early detection during antenatal care and by increasing access to hospital care for preeclamptic women. To decrease mortality, prediction of preeclampsia should be done timely. Early prediction of preeclampsia is still a challenge. Several markers have been studied by researchers in the past. Based on the literature review PlGF and uterine artery doppler have shown promising results in the prediction of preeclampsia. However, most of the studies available were conducted

on the Caucasian and African American population. Data from the South Asian population is still insufficient and needs supplementation with studies.[8]

PIGF is an angiogenetic protein which is a member of the sistein knot amino acids family. PIGF is especially synthesized by the placenta in the advancing weeks of gestation. Apart from gestation, PIGF expression increases with diseases such as ischemic heart disease or myocardial infarction. PIGF coordinates the activation of vascular endothelial growth factor (VEGF) which is the most potent of all angiogenetic inductive molecules. Angiogenesis is the development of the vascular network by remodeling of the primer capillary plexus. VEGF and VEGF-like proteins are efficacious in this molecular complex phenomenon. VEGF is the most potent angiogenetic factor and induces the main two steps of vascular network development: the proliferation of the endothelial cells and their migration. The VEGF family is formed of six different molecular-shaped proteins: VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E, and PIGF. PIGF contains 40 % similar aminoacid repetition to VEGF. The heterodimers of PIGF and VEGF are formed naturally and they are mitogenic to endothelial cells. The different pathophysiologic roles of different forms of PIGF are regulated by fms-like tyrosine kinase receptor-1. PIGF is expressed primarily in placental tissue and specifically by trophoblastic cells. Invitro studies determined that hypoxia has an inducing effect on VEGF and reducing effect on PIGF expression.[9]

In a prospective study by Boutin et al in 2019, out of 4,652 participants at a false-positive rate of 10%, PlGF combined with maternal characteristics could have predicted 26% of term and 55% of preterm PE.[10]

It is possible to predict significant vascular events and preeclampsia early in pregnancy through uterine artery Doppler (UAD). From the implantation stage to the end of pregnancy, detecting changes in uterine and placental blood vessels can provide a favorable diagnostic instrument for pregnancy complications. Quantitative parameters can identify abnormal uterine

artery recasting and decreased uterine artery blood flow, and find high-risk pregnant women who are likely to face adverse pregnancy outcomes. Uterine placental vascular impedance gradually declines during angiogenesis and stabilizes after 24 gestational weeks. The reduction of placental blood perfusion may occur again in the successive pregnancy. The pulsatility index (PI), resistance index (RI), systolic/diastolic (S/D) ratio, and the appearance of an early diastolic notch are common indicators to evaluate uterine artery blood flow. Under-developed countries should seek advanced means to adjust the current strategy, benefiting more people. UAD is such an economical approach, which may provide a novel method to forecast PE and FGR in under-developed countries.[11]

Oancea et al in 2020 in a prospective research involved 120 Caucasian pregnant women with high-risk factors for PE at 11–14 gestational weeks. Accordingly, the predictive sensitivity of UtA-PI for PE was 61.5%, and the specificity was 63.8%.[12] A meta-analysis by Velathaur et al in 2014 explored the predictive effect of UAD on PE and FGR in early pregnancy. The authors assessed 55,974 females in 18 studies, and 15 of them were performed among low-risk pregnant females. In early pregnancy, the predictive sensitivity of anomalous UAD on PE and early-onset PE was 26.4 and 47.8%, respectively. Moreover, 15.4% of FGR could be forecasted, and the prediction sensitivity of early-onset FGR was 39.2%. As an independent index, UAD has a medium predictive effect in the low-risk population in the first trimester, around 40–70%. The prediction ability for early-onset PE can reach more than 90% using the multi-parameter prediction model, including UtA-PI, maternal characteristics, and biochemical indices.[11]

Aneuploidy is the presence of abnormal number of chromosomes in a cell and occurs in 1 in 160 live births.[13] Most common aneuploidies are trisomies which form 0.3% of live births. Most common trisomy involves chromosome 21 or Down’s syndrome. The estimated incidence of Down syndrome is between 1 in 1,000 to 1 in 1,100 live births worldwide.[14] In

India every year, about 6,000 babies are born with Down syndrome, which is about 1 in every 700 babies born.[15] It causes intellectual disability, cardiac disorders, gastrointestinal and other organ dysfunctions. Other trisomy include Patau syndrome (trisomy 13) and Edwards syndrome (trisomy 18). Monosomy is another type of aneuploidy in which there is a missing chromosome. A common monosomy is Turner syndrome, in which a female has a missing or damaged X chromosome.[16]

In the first trimester of pregnancy, screening by a combination of ultrasound markers (the nuchal translucency -NT) and maternal serum biomarkers β-hCG (human chorionic gonadotropin) and PAPP-A (pregnancy associated plasma protein - A) can identify up to 97% of fetuses with trisomy 21 and other major chromosomal abnormalities.[17] NT measurement alone has a detection rate for Down Syndrome (DS) of 70% with a 5% false positive rate.[18] Prenatal diagnosis of chromosomal abnormalities is currently accomplished by invasive techniques, such as amniocentesis and chorionic villus sampling (CVS). The diagnostic accuracy of karyotyping with amniocentesis is 99.4–99.8% and for CVS is 97.5–99.6%.[19]

In an effort to have a combination strategy to predict preeclampsia and aneuploidy in 2020 Fetal Medicine Foundation used an algorithm-based screening method, combining maternal factors, mean arterial pressure, uterine-artery pulsatility index, and PlGF which demonstrated a detection rate of 94.1% at a false positive rate of 10% and a negative predictive value of 99.98%.[20]

Several screening models have been developed to identify pregnancies at high risk for PE at 11–13 weeks of gestation. These are mainly multiparametric algorithms derived from logistic regression analysis combining maternal characteristics and medical and obstetric history (the so-called a priori risk) with a series of biophysical and biochemical markers (expressed as multiples of gestational age–specific multiples of the median [MoMs] and log-10 transformed to make their distribution

Gaussian) using their likelihood ratios (LR) or regression coefficients to obtain a patient-specific a posteriori risk for PE. Although these multiparametric algorithms have shown high sensitivity for the prediction of PE, they have shown a poorer performance when applied to populations other than the population from which they were derived.[20]

Serum PAPP-A can also be used in screening for PE but the performance is lower than with the use of PlGF, and if PlGF is used in combination with maternal factors, mean arterial pressure and uterine artery pulsatility index, there is no additive value from the use of PAPP-A. Both serum PAPP-A and PlGF at 11–13 weeks' gestation is reduced in pregnancies with fetal trisomy and in those that subsequently develop PE. In screening for PE, the preferred biochemical marker is PlGF, whereas in screening for trisomy, the established marker is PAPP-A. The objective of this study was to examine the impact of adding PlGF in first-trimester biochemical screening for aneuploidies, because such policy could potentially minimize the cost and achieve effective screening for both trisomy and PE.[21]

This combination can provide accurate information regarding short- and long-term prognosis, recurrence risk, counselling and optimizing the outcome in preeclampsia and aneuploidy.

This study is an attempt to show early prediction of preeclampsia. This will help in timely management and reduction of maternal adverse events due to preeclampsia.

Moreover, this will also evaluate risk assessment for aneuploidy and may enhance the screening performance of combined first trimester screening.

AIMS AND OBJECTIVES

To study the predictive value of first trimester screening combined with PlGF and Uterine artery Doppler for preeclampsia and aneuploidy.

REVIEW OF LITERATURE

Preeclampsia (PE) is the second single leading cause of maternal mortality. Preeclampsia is responsible for over 70 000 maternal deaths worldwide every year which accounts for 14% of maternal deaths worldwide and 29.54% of maternal deaths in India.[22][23]

Preeclampsia is a multi-system disorder characterized by new onset hypertension (Systolic Blood Pressure ≥140 mmHg and Diastolic Blood Pressure ≥ 90 mm Hg) and proteinuria (≥300 mg/24 hours) occurring after 20 weeks of gestation in a previously normotensive woman.[24][25]

Mild preeclampsia present with mild hypertension (≥140/90 &<160/110 mmHg) and proteinuria ≥ 300 mg/24 hours. Severe pre-eclampsia has been characterized by one or more of the following criteria: sustained systolic BP ≥ 160 mmHg or diastolic BP ≥ 110 mmHg while on bed rest, proteinuria (≥ 3 g/24 hours or 3+ on urine dipstick), oliguria, blurring of vision, pulmonary edema, epigastric or right upper quadrant pain, thrombocytopenia, and fetal growth restriction.[25][26]

The onset of clinical manifestations of preeclampsia can be varied. Majority are “late onset preeclampsia, that present after 34 weeks of gestation especially in the peripartum period. Around 10% present before 34 weeks of gestation as “early onset preeclampsia”. Few cases present as “Postpartum preeclampsia” that occurs more than 48 hours of delivery but less than four weeks after delivery.[25]

The main etiology of preeclampsia is impaired invasion of the spiral arterioles by the trophoblastic villi leading to reduced placental perfusion and release of pro-inflammatory mediators causing platelets activation, maternal renal dysfunction, generalized endothelial damage and abnormal oxidative stress and contributing to preeclampsia pathogenesis.[27]

According to Rolnik DL et al’s 2017 study, there has been increased interest in **predictive biomarkers** for preeclampsia. An effective predictive test would facilitate early diagnosis, targeted surveillance and timely delivery. A biomarker able to predict high risk women in *early*

pregnancy has clinical utility in preventing preterm preeclampsia (and associated preterm birth and perinatal morbidity) through administration of low-dose prophylaxis with aspirin to reduce preterm disease.[28]

As first-trimester combined screening for fetal aneuploidy has been widely adopted, the biochemical markers used in this testing—PAPP-A and free *β*hCG—have been evaluated extensively by Heidari R et al in 2018 and Li SW et al in 2015 in their respective studies.[29][30] Wu P et al in 2015 demonstrated the distribution of disease markers proposed for the prediction of preeclampsia and other adverse pregnancy outcomes. These included soluble endoglin (sEng), soluble fms-like tyrosine kinase-1 (sFlt-1), placental growth factor (PlGF), inhibin-A, activin-A, a disintegrin and metalloprotease 12 (ADAM12), and placental protein 13 (PP13).[31]

In 2017, Chau k et al proposed that women with PE have reduced maternal serum levels of placental products. In light of this, it is not surprising that placental growth factor (PlGF) is the most discriminating biomarker for PE—and for early-onset PE in particular—that researchers have found to date.[32]

Preeclampsia is associated with abnormal placental implantation. Abnormal cytotrophoblastic invasion and abnormal remodeling of maternal uterine spiral arteries lead to pathological resistance to placental blood flow and hence, placental ischemia, resulting in various maternal and fetal effects. The reduced invasion of trophoblastic cells into the myometrial portions of the spiral arteries, leads to increased resistance to flow in the uteroplacental unit, which is transmitted upstream to the uterine arteries.The pathological changes of preeclampsia begin to appear as early as in first trimester.[33]

A descriptive observational study study by Handa et al on 200 women in 2019 showed a positive association between uterine artery pulsatility index of and development of combined FGR and preeclampsia in a pregnancy.[30] Abnormal Doppler studies in both the first and second trimesters have been reported to be associated with preeclampsia.[34][35][36]

Several guidelines exist to stratify risk using pregnancy factors and maternal characteristics. The National Institute for Health and Care Excellence (NICE) and American College of Obstetricians and Gynecologists (ACOG) guidelines list previous preeclampsia, chronic renal disease, chronic hypertension, pre-existing diabetes mellitus autoimmune disease, multifetal gestation, nulliparity, advanced age and high body mass index (albeit at differing cut-offs), family history of preeclampsia as “high” risk factors for preeclampsia.[37-47] These guidelines are easy to apply to all pregnant women without cost, or additional testing, however, perform with poor sensitivity. For example, only 41% of women destined to deliver preterm preeclampsia will be screen-positive using the NICE guidelines. Predictive performance for late gestation preeclampsia is even poorer.[47][48]

To address this gap, a new first-trimester screening algorithm has been developed and validated to predict preterm preeclampsia. It combines mean arterial blood pressure, Doppler ultrasound measured maternal uterine artery resistance, and levels of circulating Placental Growth Factor (PlGF). This test is superior in predicting preterm preeclampsia compared to clinical risk factors alone. It correctly detects 82% of cases – doubling the detection rate achieved by application of clinical factors using the NICE guidelines.[48]

Prediction of preeclampsia:

1.Placental Growth Factor:

Placental growth factor is a member of the vascular endothelial growth factor (VEGF) family and is predominantly expressed in the placenta, although it is also expressed at low levels in many other tissues, including the heart, lung, thyroid, liver, skeletal muscle and bone. The human PlGF gene is located on chromosome 14q14 and encodes 4 isoforms of PlGF. The protein is secreted as a glycosylated homodimer and also binds to neuropilin receptor-1 (NP-1) and -2 present in neurons. NP-1 has also recently been identified in placenta.[32]

Khaliq et al in 2000 reviewed the invitro studies that determined that hypoxia has an inducing effect on VEGF and reducing effect on PlGF expression. During placentation, expression of PlGF as a protein has a role in trophoblast invasion to maternal decidua. PlGF is thought to induce nonbranching angiogenesis leading to a low-resistance placental vascular network.[49] Physiological exercise induced ischaemia in skeletal and cardiac muscle does not stimulate PlGFproduction but PlGF is upregulated in pathological conditions such as coronary artery disease. Accordingly, PlGF expression is upregulated by hypoxia in non-trophoblast cells.[50]

Rath et al in 2016 compared the placental tissue and serum samples of preeclamptic patients with healthy control group and concluded that PlGF may be responsible for low oxidative stress and endothelial dysfunction, leading to pathogenesis of preeclampsia.[51]

A prospective cohort study by Boutin et al in 2017 reported two models using similar variables including first trimester PlGF and ultrasound findings could be used for early prediction of preeclampsia and identification of fetal aneuploidies.[52] Fetal trisomy 21 (down syndrome) is associated with trophoblastic hypoplasia, placental hypervascularity and low maternal serum PlGF concentrations.[53-55]

Concentrations of PlGF are low in the first trimester of an uncomplicated pregnancy and increases from week 11 to 12 onwards to a peak at week 30, after which it decreases. This is in contrast with soluble fms-like tyrosine kinase 1 (sFLT-1), which increases towards the completion of pregnancy. This normal divergence of angiogenic factors levels occurs as the bioavailability of PlGF is reduced by binding to sFLT-1. Normal PlGF concentrations are dependent on gestational age, with the lower limit of normal (defined as the 5th centile) ranging from a peak of approximately 141 pg ml^{-1} at around 30 weeks gestation to 23 pg ml^{-1} at term.[56]

In pregnancies complicated by preeclampsia, limited angiogenesis early in pregnancy with shallow vascular invasion of maternal spiral arteries leads

to subsequent placental hypoperfusion. Duhig et al in 2019 conducted a randomised controlled trial on 1035 women with suspected preeclampsia and found a significant reduction in time taken for diagnosis of preeclampsia. The study also found reduction in severe maternal adverse outcomes with the knowledge of circulating PlGF concentration in such patients.[57]

In a prospective study by Caillon et al in 2018 the serum sFlt-1/PlGF ratio showed highly predictive performances for ruling out PE. Using these biomarkers in routine management of PE may improve clinical care and avoid inappropriate hospitalization, which has a significant economic impact.[58] PlGF is abnormally low in women with preeclampsia as compared to their gestational age-matched controls.[59][9] SerumPlGF is found to be decreased in women both at the time of diagnosis with pre-eclampsia and well in advance of syndrome onset. The deficiency in PlGF is likely due to a combination of decreased expression of PlGF and reduced free PlGF due to binding with sFLT-1, which is elevated in affected women. In early pregnancy, PlGF concentrations are lower in women who subsequently develop preclampsia than in normal pregnant women, but sFLT-1 levels are no different, suggesting that PlGF expression in the placenta is decreased.[60][61]

The hypothesis that PlGF is an indicator of abnormal placentation is supported by the observation in a study by Poon et al in 2008 that women without pre-eclampsia who gave birth to small for gestational age babies had low PlGF early in pregnancy.[62]

In women who will develop pre-eclampsia, PlGF is low in the first trimester, well before the disease clinically manifests. Dover et al in 2013 documented that aPlGF value below a ROC curvedetermined cutoff was discriminatory in preeclamptic groups witha 82.2% specificity and 95.7% negative predictive value.[9]

In another study by Poon et al in 2013 on over 62,000 women with singleton pregnancies, despite the differences between groups, single

angiogenic factors were not useful for prediction with PlGF having a sensitivity of 32% for a 5% false-positive rate.[62] Kleinrouweler et al in a 2020 meta analysis reported similar statistics for PlGF.[63] In a meta analysis by Agrawal et al in 2019 the predictive value of PlGF for preeclampsia had a sensitivity of 78% and specificity of 88%.[59]

Duhig et al's economic analysis in a randomised controlled trial in 2019 supports a role for implementation of PlGF testing in antenatal services for the assessment of preeclampsia.[57]

2.Uterine Artery pulsatility index:

Uterine artery doppler examination reflects total measurable distal vascular resistance and provides information about placental volume and the cross section of placental vessels.[12]

Das et al in 2022 conducted a prospective study in 2020 at AIIMS, Raipur on 142 women and found that mean uterine artery pulsatility index in first trimester was higher in patients with preeclampsia with a sensitivity of 68% and specificity of 52.99% at a cutoff of 1.48.[23] Given the common origins of FGR and preeclampsia (Esp early onset preeclampsia) in defective placentation and consequent uteroplacental insufficiency, first trimester doppler assessment of uterine circulation has been studied in numerous populations to determine its utility in the prediction of later pregnancy complications. This can be done much before the onset of clinical features. [64]

First-trimester transabdominal UtA Doppler can be performed at the level of the internal cervical os from its ascending branch (Site A) or at the level of the apparent crossover with the external iliac vessel (Site B). In a prospective study by Lefebvre et al in 2012 it was concluded that first-trimester uterine artery doppler measurements for prediction of pre-eclampsia and FGR should be taken at the level of the internal cervical os from its ascending branch.[65]

Liao et al in 2009 concluded that Pulsatility index (PI) values using the site of crossover with external iliac vessel is not a reliable marker. Thus, site A

would be a better marker of impaired placentation process and placental-related adverse pregnancy outcomes.[65][66]

Protocol for uterine artery PI measurement via transabdominal technique:

- A 5 or 3.5-MHz curvilinear transabdominal transducer is used. A midsagittal section of the uterus and cervical canal is obtained.
- The transducer is moved laterally until the paracervical vessels are visualized. Color flow Doppler is applied. The uterine arteries are seen as aliasing vessels along the side of the cervix.
- Using pulsed wave Doppler, flow velocity waveforms from the ascending branch of the uterine artery at the point closest to the internal os are obtained, with the Doppler sampling gate set at 2 mm.
- Care is taken to use the smallest angle of insonation (<30°) in order to achieve the highest systolic and end-diastolic velocities.
- When three similar consecutive waveforms are obtained, the PI can be measured. The mean PI is calculated as the average reading from each side combined.[67][68][69]

In a prospective study by Gomez et al in 2008, uterine artery PI and RI values decrease with increasing gestational age, a change that is thought to be secondary to a fall in impedance in uterine vessels following trophoblastic invasion. The mean uterine artery PI continued to fall in the third trimester until week 34, although the prevalence of bilateral notch remains almost stable beyond 25 weeks of gestation.[70]

In 2020, Oancea et al in a prospective study on Caucasians in 2020, concluded that first trimester uterine artery Doppler examination is an effective non-invasive screening test for preeclampsia.[12]

In a study by Khong et al in 2015 the sensitivities and specificities of uterine artery Doppler indices for the prediction of preeclampsia in low risk populations vary from 34% to 76% and 83% to 93%, respectively.[69] The low sensitivity of this test limits its utility as a disease marker in isolation. Algorithms that combine maternal characteristics, uterine artery Doppler

velocimetry, and biochemical markers in the first trimester have the potential to improve the detection rate of early-onset preeclampsia to over 90% at a false positive rate of 10%. This was supported in studies by Akolekar et al in 2011 and 2013.[71][72]

Combinations of angiogenic factors with aspects of history or ultrasound findings to create multifactorial predictive tools are promising. The Fetal Medicine Foundation predictive algorithm from 2013 at 11–13 weeks gestation, which uses a combination of maternal characteristics, mean arterial pressure, uterine artery pulsatility index, PAPP-A and PlGF detects 95 and 46% of women with early and late pre-eclampsia, respectively with a false-positive rate of 10%.[73]

Salem et al in 2018 combined uterine artery pulsatility index, maternal serum PAPP-A and PlGF in a prospective study on 300 patients. The combination had a sensitivity, specificity, a positive predictive value, a negative predictive value and an accuracy of 56.7,99.3,89.5,95.4 and 67% respectively.[27]

Prediction of aneuploidy:

First trimester screening includes a combination of ultrasound for nasal bone and nuchal translucency with serum biomarkers like free β hCG and PAPP-A. These parameters when combined had sensitivity, specificity, positive predictive value and negative predictive value of 87.8%, 97.6%, 2.4% and 0.06% respectively for aneuploidy in a study by Li SW et al in 2015 on 10,289 pregnant women.[74]

1. Nuchal Translucency:

Nuchal translucency refers to the transient subcutaneous collection of fluids present behind the fetal neck and can be detected using ultrasonography at 11-14 weeks of gestation as an important ultrasonic parameter during the first trimester of pregnancy.[75]

Heidari et al conducted a retrospective case control study on 6384 women in 2018 where using an increased NT as the sole criteria for fetal aneuploidy screening detects approximately 77% of fetuses with trisomy

21.[29] An increased NT thickness is associated with adverse pregnancy outcomes, including a higher risk of chromosomal and structural abnormalities. Invasive prenatal diagnostic techniques can be used to exclude chromosomal anomalies when an abnormal fetal NT thickness is detected.[76][77] As an indicator in the first trimester, NT is closely related to the risk of fetal chromosomal abnormalities, however as a single indicator, its screening ability is limited.[75-79]

Fetal NT measurements are independent of maternal serum levels of hCG and PAPP-A; therefore, these markers can be combined into a single screening test. The combination of free β-hCG or hCG, PAPP-A, and NT with maternal age is able to detect approximately 80–85% of fetuses with trisomy 21 at a false-positive rate of 5% as was studied by Heidari R et al in 2018.The cutoff used to determine an abnormal NT varies between gestational-age cut-offs for the 95th percentile and 3.0 mm.[29][75-79]

2. Biochemical markers for aneuploidy

In screening using maternal serum biochemical markers, the measured concentration of the markers is converted into MoM of unaffected pregnancies at the same gestation as was done in studies by Heidari et al in 2018 and Li SW et al in 2015 in their respective studies.[29][74] This is to allow for the fact that marker levels vary with gestational age.[80][81]

Free B hCG (Human Chorionic Gonadotrophin) and PAPP-A (Pregnancy Associated Plasma Protein):

Human chorionic gonadotropin is a 39,500-Da glycoprotein hormone normally found in blood and urine only during pregnancy.[80][82]

The overall data suggest that free *β*-hCG has slightly increased sensitivity when compared with intact hCG. Free *β*-hCG and intact hCG levels are reduced in trisomy 18.[83-87] Aldredet al. in a 2015 Cochrane review reported elevated levels of maternal serum hCG in Down's syndrome pregnancies.[88] Maternal serum hCG peaks at 8–10 weeks and then declines to reach a plateau at 18–20 weeks of gestation and remains quiet constant until term.[80]

PAPP-A is a glycoprotein which was originally found by Lin et al. in the plasma of pregnant woman. The protein is secreted as a disulfide-bound homodimer with a molecular weight of 400 kDa.[80] PAPP-A is one of the two maternal serum markers currently used for screening between 10 and 14 weeks. It is produced by the placental syncytiotrophoblast and decidua.[80][89] PAPP-A is also expressed in ovarian granulose cells, and in non-reproductive tissues, such as fibroblasts, osteoblasts and vascular smooth muscle cells.[80]

In normal pregnancy, the concentration of PAPP-A in maternal circulation increases with gestational age. Its concentration increases exponentially with a doubling time of 3–4 days during the first trimesters, then the level continues to rise throughout pregnancy until delivery.[80]

In a study by Durković J et al on 340 women in 2018 decreased levels of PAPP-A are found in association with down syndrome which has formed the basis for the first trimester screening. Low first trimester maternal serum levels are found not only in trisomy 21, trisomy 18 and trisomy 13, but also in non-Down syndrome fetal aneuploidies.[90]

In cases of Down's syndrome, the first trimester serum β-hCG level is increased to approximately 2.0 MoM, and the PAPP-A level is decreased to, approximately 0.5 MoM. With trisomy 18 and trisomy 13, levels of both serum biochemical marker are decreased.[91-93]

A study by Heidari R et al in 2018 on 6384 women demonstrated that when used as a single marker, at a fixed 5% false positive rate, the best estimates for detection of cases with trisomy 21 was 81% for free β-hCG and 69% for PAPP-A for specimens collected between the 10- and 14-week period. When the two markers are combined together with maternal age, the detection rates increase to 92%.[29]

In a case control study by Ozdamar O et al in 2014 ,in the pre-eclampsia group, the median PAPP-A MoM was significantly reduced whilst the median free β-hCG MoM was not different from controls. With decreasing levels of PAPP-A, the likelihood ratio for pre-eclampsia increased.[94] At

the 5th centile of normal (PAPP-A MoM 0.415) the odds ratio was increased 4-fold and at this cut-off 15% of cases of pre-eclampsia would be identified.[95]

MATERIALS AND METHODS

SOURCE OF DATA

A hospital based; prospective clinical study was conducted on randomly selected patients between 11-13^{+6} weeks period of gestation in the department of obstetrics and gynecology from 1^{st} March 2021 to 31^{st} March 2022 at Dayanand Medical College and Hospital, Ludhiana (Punjab), a tertiary care hospital.

Inclusion criteria

- All pregnant patients in first trimester between 11-13^{+6} weeks of gestation.
- Singleton pregnancies
- Non smokers

Exclusion criteria

- Multiple pregnancies
- Molar pregnancies
- Smokers
- Chronic hypertensive
- Patients on aspirin for any indication

METHODS OF COLLECTION OF DATA

The current study was conducted on 90 antenatal women who presented in OPD of department of obstetrics and gynaecology at Dayanand medical college, Ludhiana. The study was approved by the Ethical Committee and Faculty of Medical Sciences. A detailed history was taken and clinical examination was done after obtaining informed consent.

Maternal characterstics, medical and obstetric history were recorded at the first antenatal visit. The following maternal characterstics were recorded: age; height (centimeters); weight (kilograms), level of education and socioeconomic class, ethnicity, smoking habits. Medical disorders including diabetes mellitus, renal disease, autoimmune disease, thalassemia were noted. Obstetric history variables included gravidity and a history of preeclampsia.

Blood pressure was measured at 11 weeks to 13^{+6} weeks with a calibrated OMRON HEM automated device, randomly in the right arm or left arm after a 5 min rest in the seated position. Mean arterial pressure (MAP) was calculated as diastolic BP+ (systolic BP-diastolic BP)/3.

Routine investigations were performed for all patients in the first antenatal care visit including CBC, Rh, bloodgroup, random blood sugar, TSH, VDRL, HbA2 analysis. Maternal serum levels of placental growth factor (PlGF), pregnancy associated plasma protein (PAPP-A) and β human chorionic gonadotropin (β-hCG) all were measured with the ECLIA (Electro chemiluminescence Immunoassay) by Roche e411. The results of β hCG and PAPP-A were expressed as multiple of median (MoM) for gestational age. It was adjusted according to the demographic parameters like age, ethnicity, smoking status, BMI, gravidity and gestational age. The patient specific risks were calculated by multivariate likelihood approach. Using the cutoff of 1:250 for trisomy 18, trisomy 21, trisomy 13 patients were divided into low and high risk groups. High risk patients were offered genetic counselling and prenatal testing. Performance of biochemical markers alone and in combination with ultrasound was studied.

Maternal serum assays for PlGF was done using Elecsys electro chemiluminescence Immunoassay (ECLIA) for the invitro quantitative determination of PlGF in human serum. The measuring range of assay was 3 pg/ml – 10,000 pg/ml. The serum was collected in vacutainers containing separating gel & centrifuged to separate serum. The analyzer used was COBAS 8000 (Roche Diagnostics) automated to calculate the analyte concentration of each sample in pg/ml.

Using ultrasound, uterine artery doppler evaluation was performed at 11weeks to 13^{+6} weeks by transabdominal technique. A 5 or 3.5-MHz curvilinear transabdominal transducer was used. A midsagittal section of the uterus and cervical canal was obtained. The transducer was moved laterally until the paracervical vessels are visualized. Color flow Doppler was applied. The uterine arteries were seen as aliasing vessels along the

side of the cervix. Using pulsed wave Doppler, flow velocity waveforms from the ascending branch of the uterine artery at the point closest to the internal os were obtained, with the Doppler sampling gate set at 2 mm. Care was taken to use the smallest angle of insonation (<30°) in order to achieve the highest systolic and end-diastolic velocities. When three similar consecutive waveforms were obtained, the PI was measured. The mean PI was calculated as the average reading from each side combined. Nuchal translucency and presence of nasal bone were noted, gestational age was calculated using Crown Rump Length (CRL) at the same time.

Patients were followed monthly till 28 weeks then biweekly till 36 weeks and weekly thereafter. Standard antenatal protocol was offered to all patients. Blood pressure was checked on every visit. Hematinics were prescribed and immunization was administered. Anomaly scan, glucose screening test and growth scans were done. Patients were divided into two groups preeclampsia and no preeclampsia. Preeclampsia was diagnosed if BP recordings were systolic Blood Pressure ≥140 mmHg and diastolic Blood Pressure ≥ 90 mm Hg and proteinuria (≥300 mg/24 hours) occurring after 20 weeks of gestation in a previously normotensive woman. Both the groups were compared for demographic parameters like age, ethnicity, smoking status, BMI, gravidity and gestational age and risk factors like previous obstetrics complications and biochemistry of serum markers. Correlation was made with obstetrical outcome like mode of delivery and neonatal outcome like neonatal birth weight and NICU admission. Development of preeclampsia before 34weeks and after 34 weeks period of gesatation was recorded as early onset and late onset preeclampsia respectively.

DURATION OF STUDY:

The study was conducted on 90 antenatal women for a time period of 1 year, from March 2021 to March 2022.

STATISTICAL ANALYSIS:

Data were described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. To determine whether the data were normally distributed, a Kolmogorov-Smirnov test was used. Comparison of quantitative variables between the study groups was done using Mann Whitney *U* test for non-parametric data. For comparing categorical data, Chi square ($\chi 2$) test was performed and fisher exact test was used when the expected frequency is less than 5. Receiver operator characteristics (ROC) curve was done, and criterion value was estimated depending on the specificity and sensitivity. Area under curve (AUC) was measured. A probability value (*p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

In our study from March 2021 to March 2022, a total of 90 patients at 11wks to 13^{+6} weeks were recruited for combined first trimester screening with uterine artery doppler and PlGF. 4 patients were lost to follow up, and this resulted in a data of 86 patients being included in the study. The results were analysed according to:

1. Demography
2. Gestational age at screening
3. Biophysical parameters for preeclampsia:
    a) MAP,SBP,DBP
    b) Uterine artery pulsatility index
4. Biochemical parameters for preeclampsia and aneuploidy:
    a) B hCG
    b) PAPP-A
    c) PlGF
5. Prediction of preeclampsia
6. Prediction of aneuploidy

1. Demographic parameters:

The demographic parameters analysed in the study population were:

a. Age
b. Ethnicity
c. Body Mass Index (BMI)
d. Education
e. Socio economic status
f. Gravidity
g. Obstetric history
h. Risk factors

a. Age

TABLE 1: Distribution of study population according to age.

AGE GROUP	No. of cases	Percentage
<25	9	10.5%
26-30	42	48.8%
31-35	26	30.2%
> 35	9	10.5%
Total	86	100.0%

A majority of the women (48.8%) of the study population were in age group of 26-30 years and 30.2% women were from the age group of 31-35 years. The age group of <25 and >35 had 10.5% participants each. The mean age of the study population was 30.31 years with a standard deviation of 4.09.

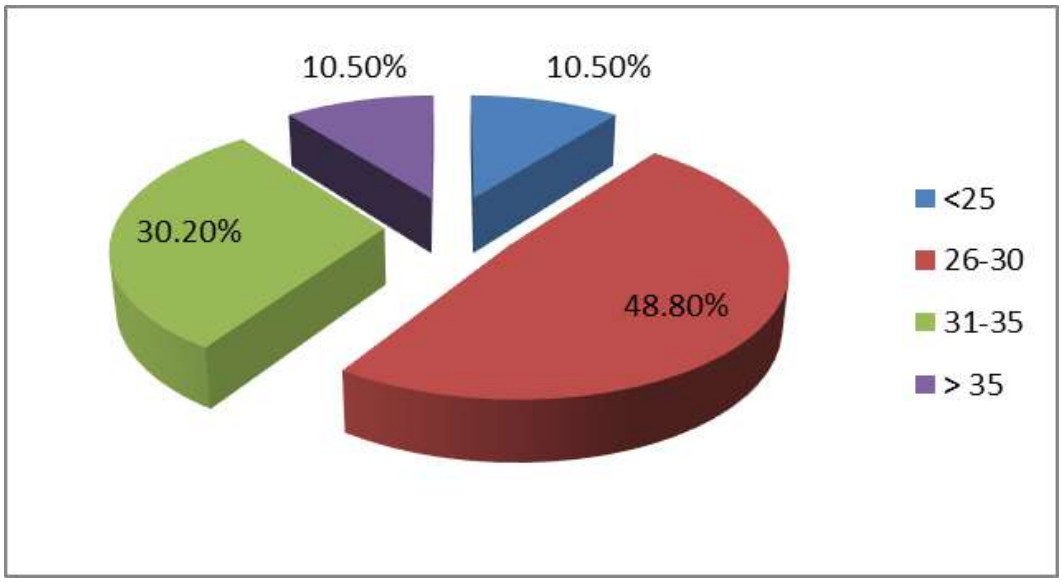

FIGURE 1: Distribution of study population according to age.

b. Ethnicity:

All patients were of Indian in origin.

c. Body mass index:

TABLE 2: Distribution of study population according to BMI(in kg/m^2).

BMI GROUP	No. of cases	Percentage
< 18.5 (Underweight)	4	4.7%
18.5-24.9 (Normal)	33	38.4%
25-29.9 (Overweight)	9	10.5%
> 30 (Obese)	40	46.5%
Total	86	100.0%

A majority of the study population (46.5%) were obese with BMI of >30 kg/m^2 and 38.4% women had a normal BMI between 18.5-24.9 kg/m^2.

Only 4 women were underweight with BMI <18.5 kg/m^2.

The mean BMI of our study population was 25.42 kg/m^2 with a standard deviation of 3.32.

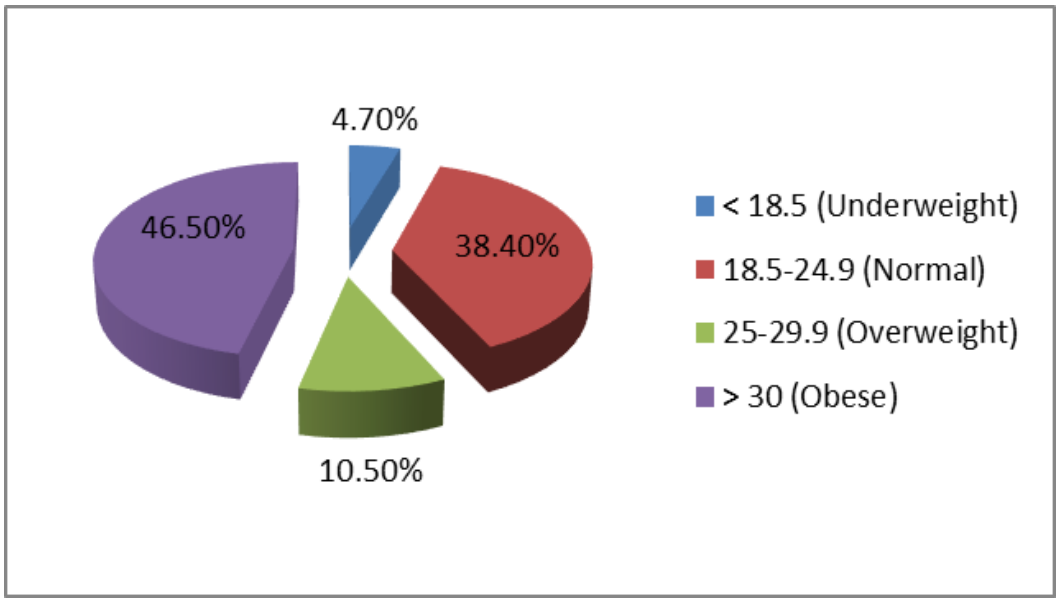

FIGURE 2: Distribution of study population according to BMI(in kg/m^2).

d. Education

TABLE 3: Distribution of study population according to education.

	Number of cases	Percentage
Postgraduate	11	12.7%
Graduate	60	69.7%
Higher secondary	12	13.9%
Secondary	03	3.5%
Primary	00	0%
Total	86	100%

A majority of the study population 69.7% were graduates followed by 12.7% women were postgraduates. Women with higher secondary education were 13.9%. Only 3.5% studied till secondary level. There were no participants who had only a primary level of education.

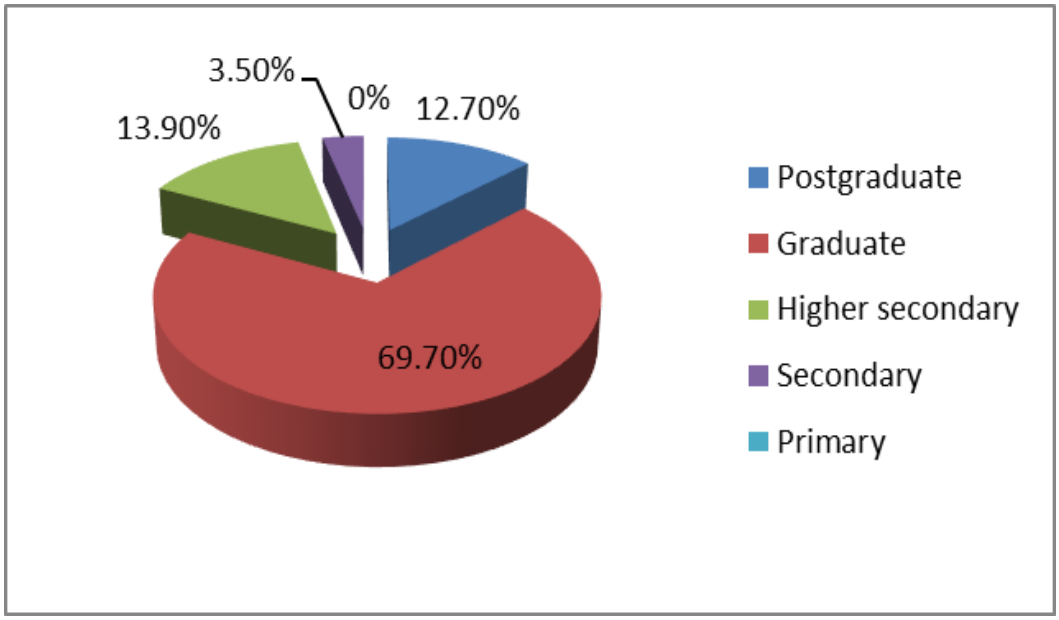

FIGURE 3: Distribution of study population according to education.

e. Socio-economic status:

The socio-economic status of the study population was decided according to modified kuppuswamy scale.

TABLE 4: Distribution of study population according to modified kuppuswamy scale.

	Number of cases	Percentage
Upper	08	9.3%
Upper middle	60	69.7%
Lower middle	10	11.6%
Upper lower	02	2.3%
Lower	06	6.9%
	86	100%

A majority of women of the study (69.7%) belonged to upper middle class and 9.3% women belonged to upper class. Out of 86 women, 11.6% were a part of lower middle class and 2.3% women belonged to upper lower class. Only 6.9% women were from lower class.

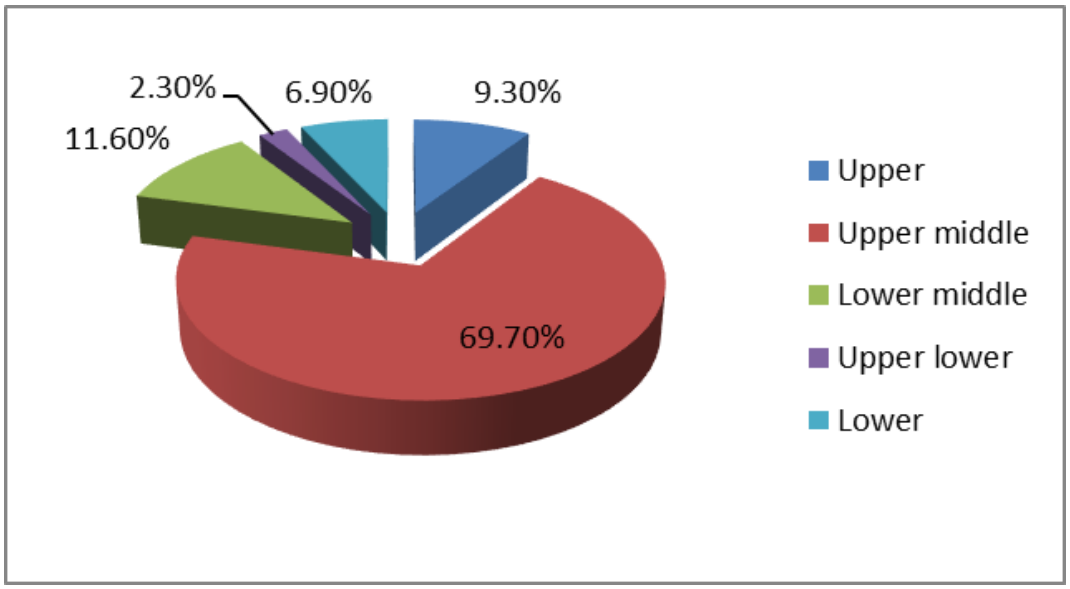

FIGURE 4: Distribution of study population according to modified kuppuswamy scale.

f. Gravidity:

TABLE 5: Distribution of the study group according to gravidity.

OBSTETRIC FORMULA	No. of cases	Percentage
Multiparous	48	55.8
Nulliparous	38	44.2
Total	86	100

Of the 86 women in the study group, 55.8 % were multigravida and 44.2 % were primigravidas.

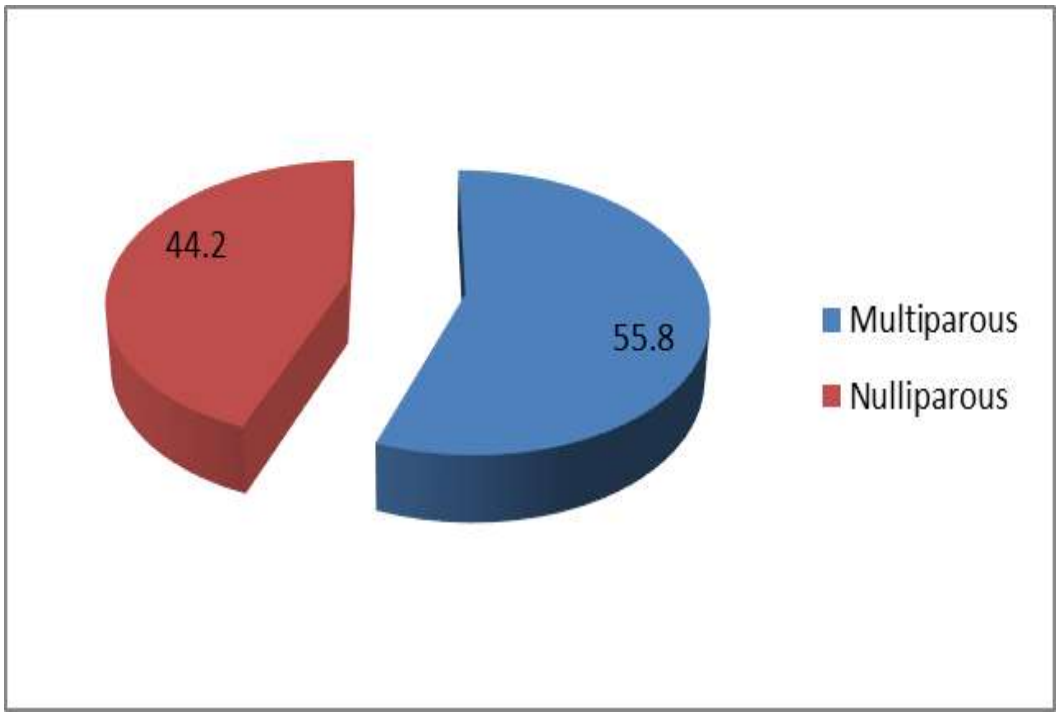

FIGURE 5: Distribution of the study group according to gravidity.

g. Obstetric history:

TABLE 6: Distribution of study group according to previous obstetric history.

OBSTETRIC HISTORY	No of cases	Percentage
Previous PE	2	2.3
Neonatal death	1	1.2
Neonatal FGR	0	0.0
No complications	83	96.5
Total	86	100

Of the total 86 cases in the study population 2 (2.3%) had a history of previous preeclampsia. There was only one neonatal death in the obstetric history of the study population. 83 patients (96.5%) had no complications previous pregnancies.

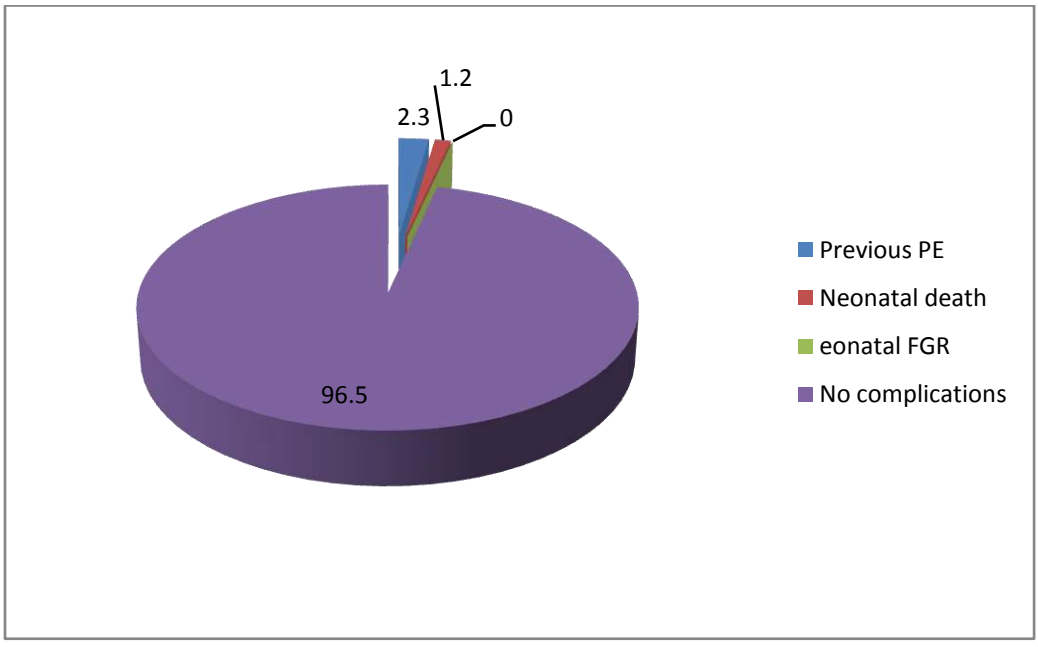

FIGURE 6: Distribution of study population according to modified kuppuswamy scale.

h. Risk factors:

TABLE 7: Risk factors in the study population.

RISK FACTORS	No of cases	Percentage
Thalassemia minor	1	1.2
Tuberculosis	1	1.2
Diabetes	0	0.0
Chromosomal abnormalities	0	0.0
Genetic disorders	0	0.0
Others	2	2.3
None	82	95.3
Total	86	100

The study population had only one case of thalassemia minor and tuberculosis each (1.2% each) with no history of diabetes, chromosomal abnormalities and genetic disorders in any of the 86 women. One of the patients had SLE and another patient had rheumatoid arthritis making up 2.3% of the total study population.

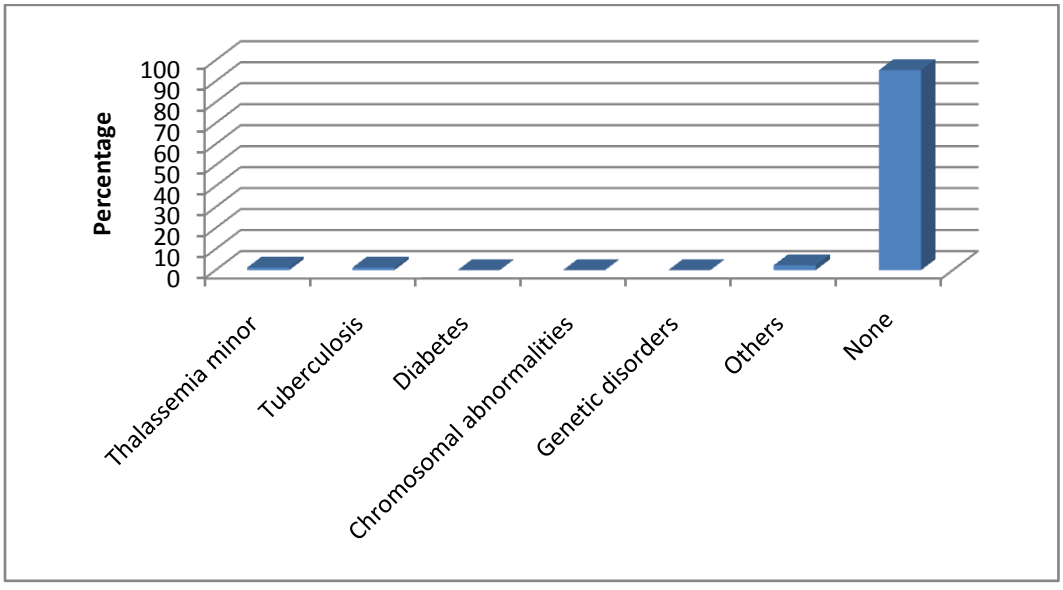

FIGURE 7: Risk factors in the study population.

2. Gestational age of first trimester screening:

TABLE 8: Distribution of study population according to gestational age of first trimester screening.

GESTATIONAL AGE GROUP	No. of cases	Percentage
11-11^{+6}	14	16.3%
12-12^{+6}	57	66.3%
13-13^{+6}	15	17.4%
Total	86	100.0%

A majority of women i.e. 66.3% were screened between 12 weeks to 12^{+6} weeks and 17.4% were screened between 13 weeks and 13^{+6} weeks. Only 16.3% women were screened between 11 weeks and 11^{+6}weeks. The mean gestational age of the study population at the time of screening was 12^{+3} weeks with a standard deviation of 0.60.

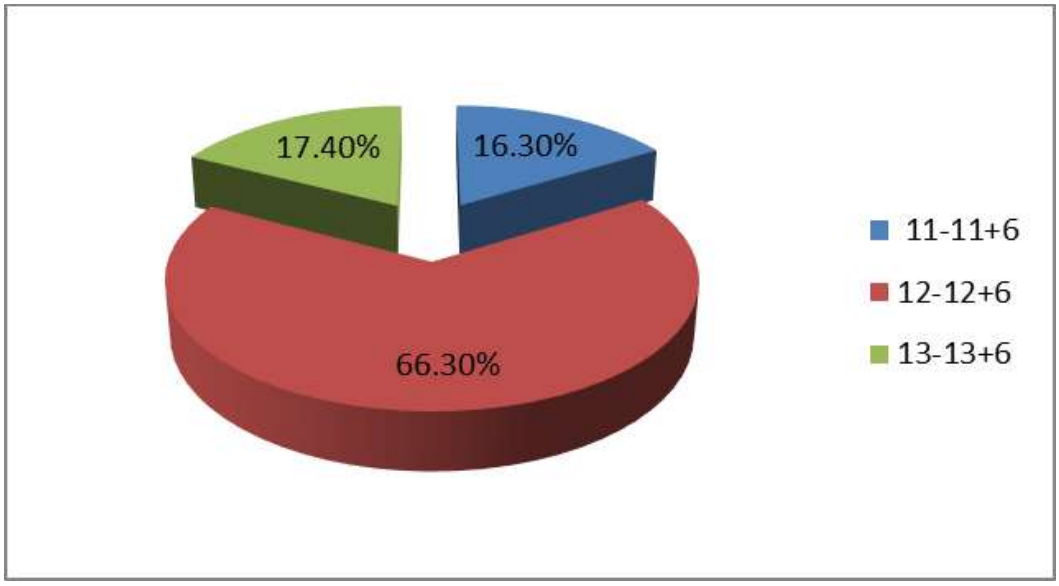

FIGURE 8: Distribution of study population according to gestational age of first trimester screening.

3. Biophysical parameters for preeclampsia:

The biophysical parameters analyzed in the study population were

I. Blood pressure
II. Uterine Artery Doppler for pulsatility index (PI).

The results were as mentioned below.

i) Blood pressure:

Blood pressure findings were analysed under 3 parameters:

a. Systolic blood pressure (SBP)
b. Diastolic blood pressure (DBP)
c. Mean arterial pressure (MAP)

a) Systolic blood pressure (SBP):

The mean Systolic Blood Pressure of the study population was 126.21 mm hg with a standard deviation of 4.09.

b) Diastolic blood pressure (DBP):

The mean Diastolic Blood Pressure of the study population was 81.86 mm hg with a standard deviation of 12.23.

c) Mean arterial pressure (MAP):

The Mean Arterial Pressure of the study population was 96.47 mmhg with a standard deviation of 14.58.

TABLE 9: Mean systolic blood pressure, mean diastolic blood pressure and mean arterial pressure of the study population (n=86).

Blood pressure	Mean n=86	SD
SBP (mmhg)	126.21	20.46
DBP (mmhg)	81.86	12.23
MAP (mmhg)	96.47	14.58

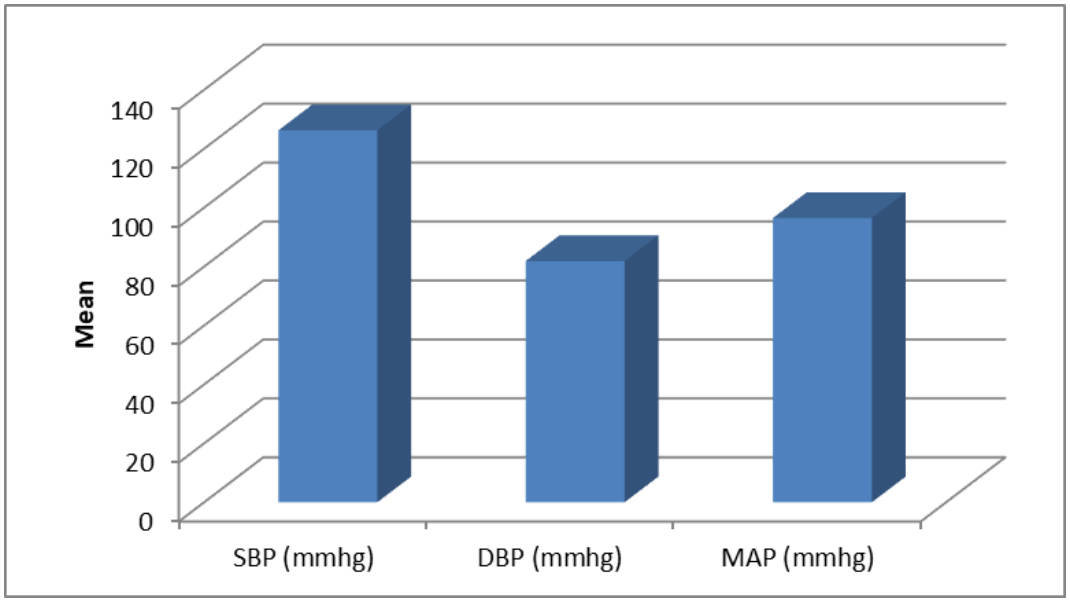

FIGURE 9: Mean systolic blood pressure, mean diastolic blood pressure and mean arterial pressure of the study population (n=86).

ii). Uterine Artery Doppler:

On transabdominal ultrasound the uterine artery pulsatility index of left and right uterine artery was taken respectively and an average of both was calculated in all 86 patients of the study population.

UTERINE ARTERY PULSATILITY INDEX (PI):

TABLE 10: Median with interquartile range (IQR) pulsatility index of left, right uterine arteries and average PI of the study population (n=86).

	Median (n= 86)	IQR
Left Uterine Artery PI	1.55	1.10-1.80
Right Uterine Artery PI	1.40	0.90-1.88
Mean Uterine Artery PI	1.44	1.1375-1.8075

The median left uterine artery pulsatility index of the study population was 1.55 with an interquartile range of 1.1-1.8.

The median right uterine artery pulsatility index of the study population was 1.40 with an interquartile range of 0.90-1.88.

The median value of average uterine artery pulsatility index (mean of left and right uterine artery PI) of the study population was 1.44 with an interquartile range of 1.13-1.80.

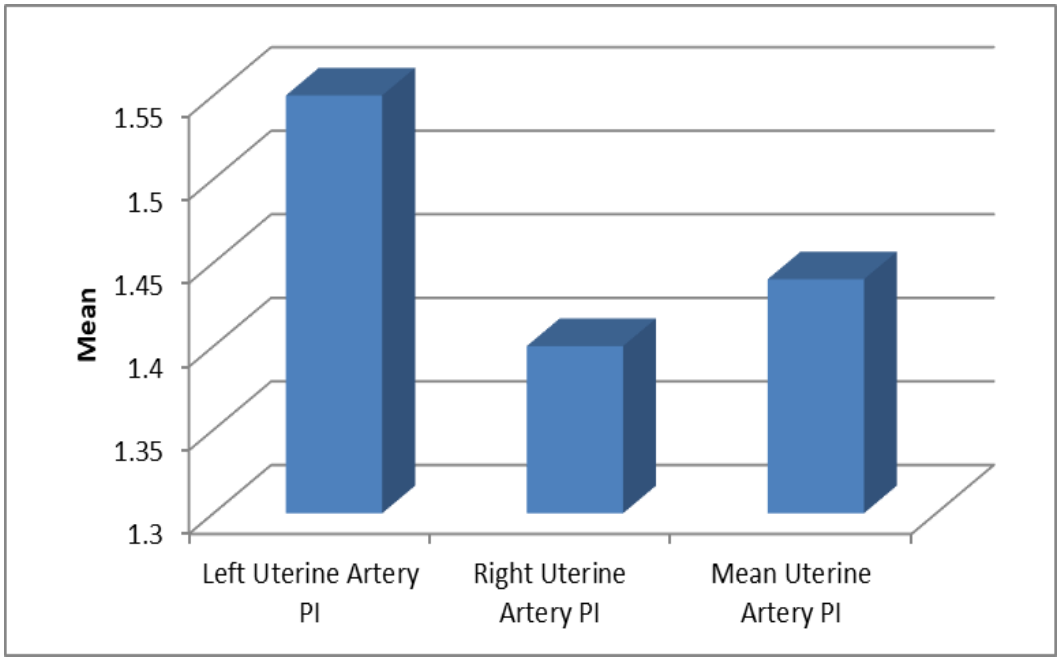

FIGURE 10: Median with interquartile range (IQR) pulsatility index of left, right uterine arteries and average PI of the study population (n=86).

4. BIOCHEMICAL PARAMETERS FOR PREECLAMPSIA AND ANEUPLOIDY:

The biochemical parameters studied in the population were

1. Free β-human chorionic gonadotropin (β-hCG)
2. Pregnancy Associated Plasma Protein (PAPP-A)
3. Placental Growth Factor (PlGF)

1. **Free β-hCG:**

The median MoM of free β-hCG in the study population was calculated as 0.98 with an interquartile range of 0.58-1.25.

2. **Pregnancy Associated Plasma Protein (PAPP-A):**

The median MoM of PAPP-A in the study population was 0.88 with an interquartile range of 0.6275-1.2.

3. **Placental Growth Factor (PlGF)**:

The median PlGF of the study population was 47.40 pg/ml with an interquartile range of 35.01-70.2.

TABLE 11: Median values free β-hCG, PAPP-A AND PlGF with interquartile range in the study population.

Biochemical variables:	Median n=86	IQR
Free β-hCG (MoM)	0.98	0.58-1.25
PAPP-A (MoM)	0.88	0.6275-1.2
PlGF (pg/ml)	47.40	35.015-70.26

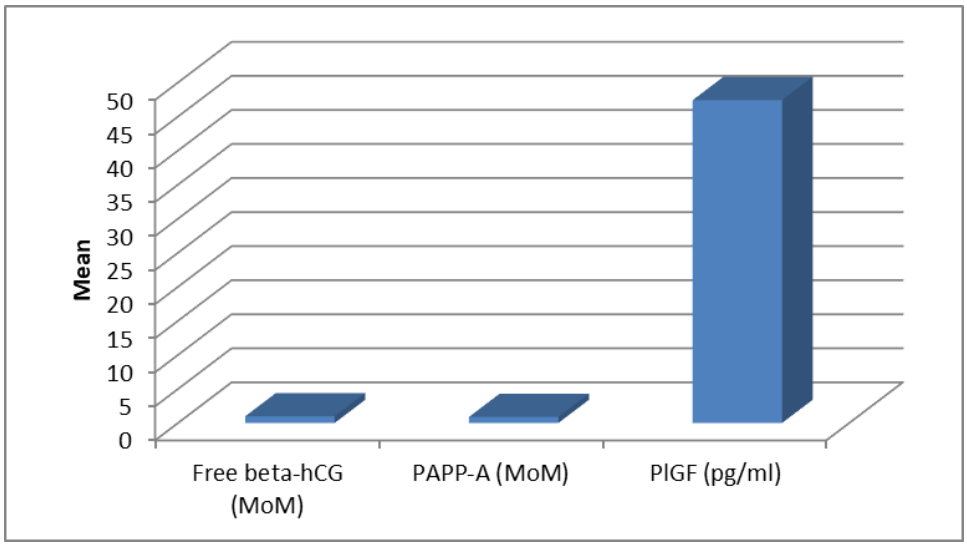

FIGURE 11: Median values free β-hCG ,PAPP-A AND PlGF with interquartile range in the study population.

5. Prediction of Pre-eclampsia:

The study population (n=86) was divided into two groups based on development of preeclampsia after 20 weeks.

Group A (n=11) had the patients who subsequently developed preeclampsia (PE) and Group B (n=75) had patients who did not develop preeclampsia (No PE).

a) Development of preeclampsia
b) Comparison of group A (PE) and group B (no PE)

a. Development of preeclampsia:

TABLE 12: Distribution of study population according to development of pre-eclampsia.

	No. of cases	Percentage
PE (Group A)	11	12.7%
No PE (Group B)	75	87.2%
Total	86	100.0%

Of the 86 patients, 11 developed pre-eclampsia (12.7%) and 75 did not develop preeclampsia (87.2%).

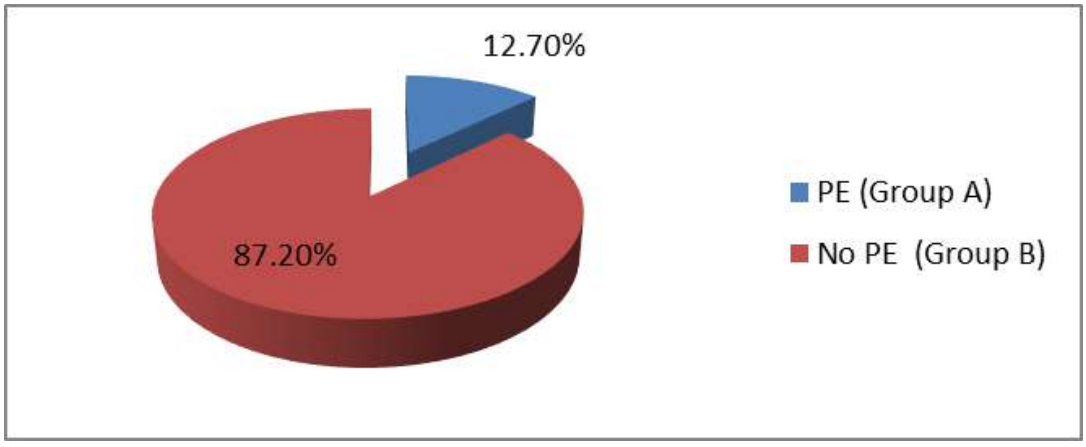

FIGURE 12: Distribution of study population according to development of pre-eclampsia.

TABLE 13: Distribution of study population according to gestation of development of pre-eclampsia.

Preeclampsia (Group A)	No. of cases	Percentage
EOPE (<34 weeks)	07	63.6%
LOPE (> 34weeks)	04	36.3%
Total	11	100%

Of the 11 patients with preeclampsia 7 (63.6%) developed early onset preeclampsia (EOPE) and 4 (36.3%) developed late onset preeclampsia (LOPE).

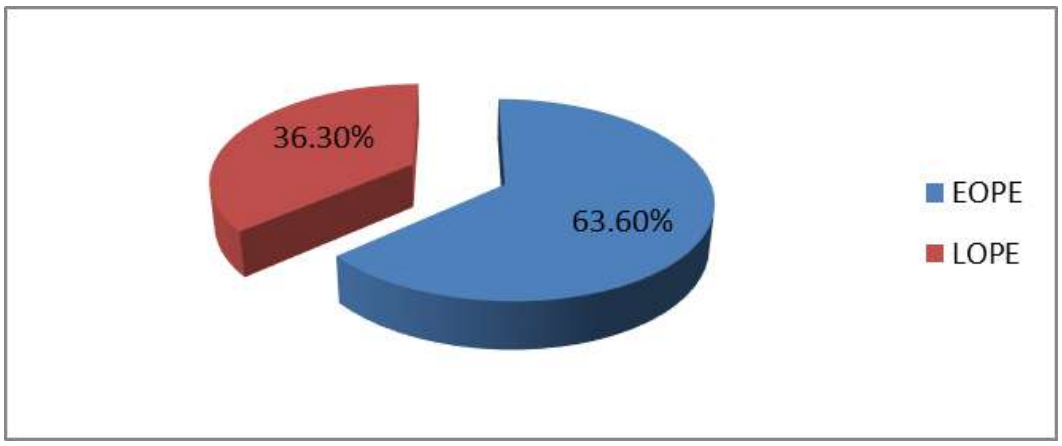

FIGURE 13: Distribution of study population according to development of pre-eclampsia.

b. Comparison of group A (PE) and group B (no PE) :

A. Demography (Age, BMI, gravidity, previous preeclampsia)

B. Biophysical parameters

C. Biochemical parameters

D. Obstetric and neonatal outcome

E. Performance of screening

A. Demographic parameters:

The demographic parameters include age, BMI, gravidity, previous history of preeclampsia and medical disorders. These parameters are discussed below:

i)Age:

TABLE 14: Distribution of study population of preeclampsia and no preeclampsia according to age.

	Group A (PE)		Group B (No PE)		Chi-square value	p-value
Age (years)	n=11	%	n= 75	%		
<25	1	9.1%	8	10.7%	0.063	0.802
26-30	6	54.5%	36	48.0%	0.165	0.685
31-35		27.3%	23	30.7%	0.052	0.819
> 35	1	9.1%	8	10.7%	0.025	0.873

The mean age of study population was 30.31 years with a standard deviation of 4.09. The mean age of the preeclampsia group was 30.18 years with a standard deviation of 1.74 vs a mean age of 30.33 years with a standard deviation of 4.16 in no preeclampsia group.

In our study, 9.1% vs 10.7% of the population belonged to age < 25 years in group A and group B respectively and this was statistically insignificant (p value 0.802).

Of the population between 54.5% vs 48% belonging to age 26-30years in group A and group B respectively and this was statistically not significant (p value 0.685).

In the age group of 31-35 years, 27.3% vs 30.7% belonged to group A and group B respectively which was statistically insignificant (p value 0.819).

Above the age of 35 years, 9.1% vs 10.7% from group A and group B respectively and this was statistically insignificant (p-value 0.873).

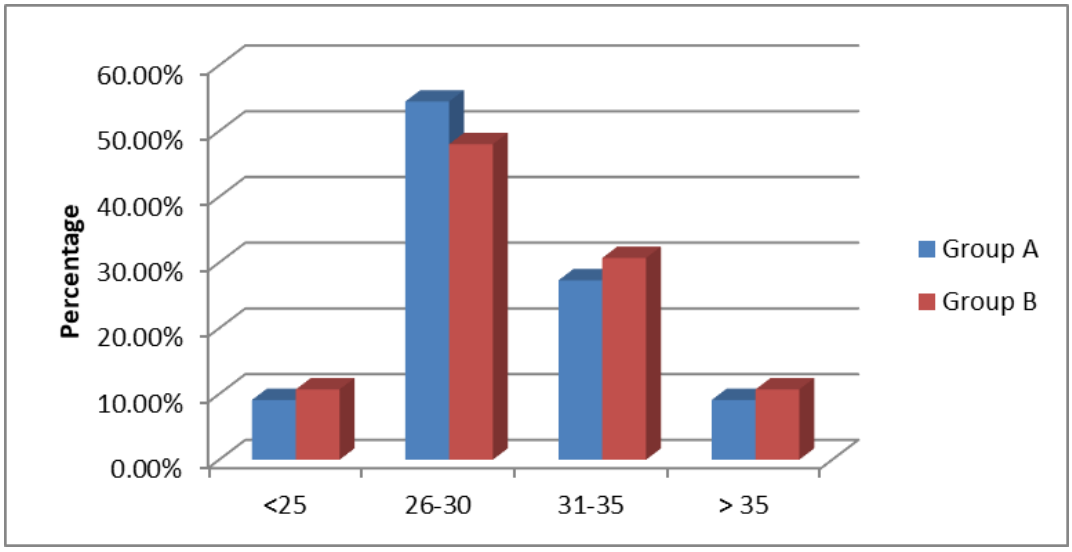

FIGURE 14: Distribution of study population of preeclampsia and no preeclampsia according to age.

ii) Body mass index (BMI):

TABLE 15: Distribution of study population of preeclampsia and no preeclampsia according to BMI.

	Group A (PE)		Group B (No PE)		Chi-square value	p-value
BMI GROUP	n=11	%	n=75	%		
< 18.5 (underweight)	0	0.0%	4	5.3%	0.615	0.432
18.5-24.9 (normal)	5	45.5%	28	37.3%	0.267	0.605
25-29.9 (overweight)	1	9.1%	8	10.7%	0.025	0.819
> 30 (obese)	5	45.5%	35	46.7%	0.006	0.94

The mean BMI in preeclampsia group was 24.57 kg/m^2 with a standard deviation of 2.25 and 25.41kg/m^2 with a standard deviation of 3.46 in no preeclampsia group.

In our study, none vs 5.3% had BMI < 18.5 in group A and group B respectively which was not statistically significant (p value:0.432).

Of the population 45.5% vs 37.3% had normal BMI group (18.5-24.9) in group A and group B respectively which was statistically insignificant (p value 0.605).

Of the population 9.1 % vs 10.7% were overweight (25-29.9) in group A and group B respectively which was not statistically significant (p value 0.819).

Of the population 45.5% vs 46.7% were obese (BMI >30) in group A and group B respectively which was statistically insignificant (p value 0.94).

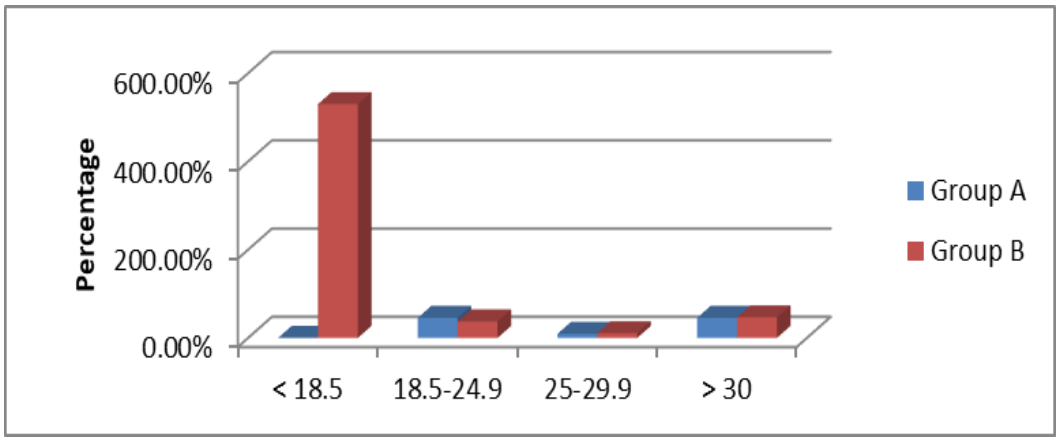

FIGURE 15: Distribution of study population of preeclampsia and no preeclampsia according to BMI.

iii). Gravidity:

TABLE 16: Distribution of nulliparous and multiparous women in preeclampsia group and no preeclampsia group.

Gravidity	Group A (PE)		Group B (No PE)		Chi-square value	p-value
	n=11	%	n=75	%		
Multi parous	3	27.3%	45	60.0%	4.166	0.054
Nulli parous	8	72.7%	30	40.0%	4.166	0.054

Of the population, 60% vs 40% of multiparous were in group A and group B respectively and this was statistically significant with a p value of 0.054. In our study, 72.7% vs 40% of nulliparous were in group A vs group B respectively with a p value of 0.054 which was statistically significant.

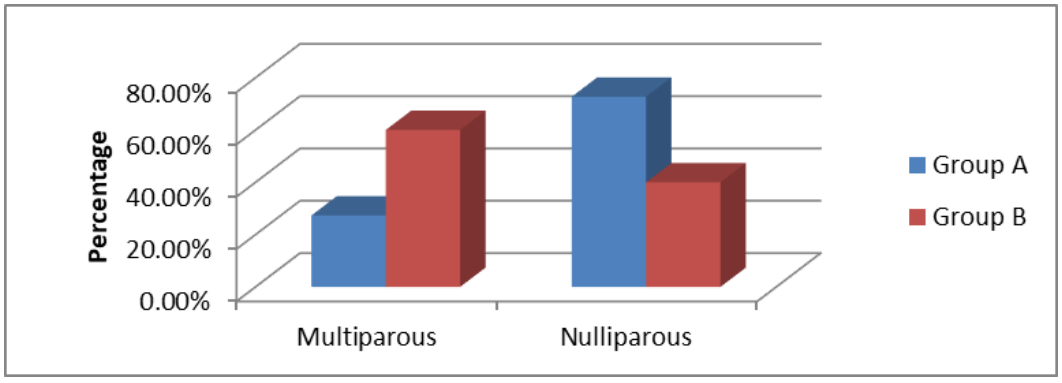

FIGURE 16: Distribution of nulliparous and multiparous women in preeclampsia group and no preeclampsia group.

4. Previous preeclampsia:

TABLE 17: Comparison of previous preeclampsia in preeclampsia group and no preeclampsia group.

	Group A (PE)		Group B (No PE)		Chi-square value	p-value
	n=11	%	n=75	%		
No previous PE	9	81.8%	75	100.0%	13.961	0.001
Previous PE	2	18.2%	0	0.0%		

Previous preeclampsia was seen in 18.2% and 81.8% had no previous preeclampsia in group A.

None of the women had previous preeclampsia in group B. All were normotensive in previous pregnancy.

This was statistically significant (p value: 0.001)

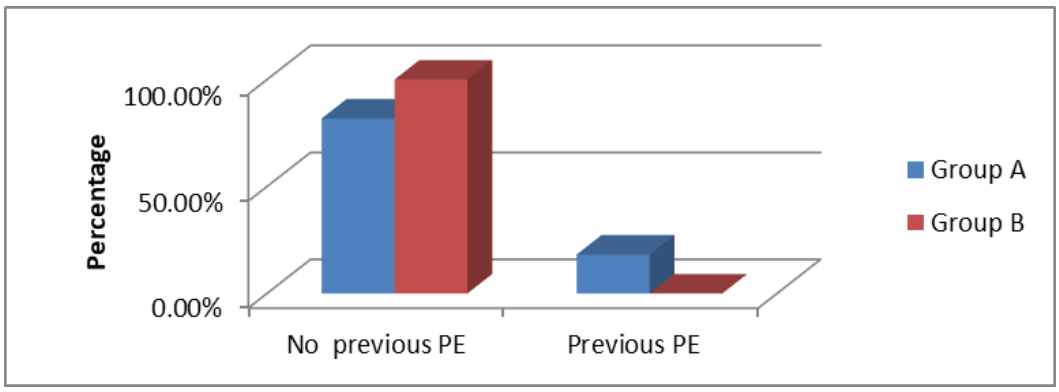

FIGURE 17: Comparison of previous preeclampsia in preeclampsia group and no preeclampsia group.

B. Biophysical parameters:

Both the groups were compared based on

1. Blood pressure readings and
2. First trimester uterine artery doppler for pulsatility index as followed.

1. Blood pressure:

The mean SBP, DBP and MAP were studied in both the groups and results were as mentioned below.

TABLE 18: Comparison of study population of preeclampsia according to Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP).

	Group A (PE)		Group B (NO PE)		Z	p-value
	Mean	SD	Mean	SD		
SBP mmHg	166.36	21.57	120.32	11.97	10.584	0.000
DBP mmHg	102.73	9.05	78.80	9.30	7.995	0.000
MAP mmHg	124.00	11.38	92.43	9.86	9.723	0.000

In our study population, the mean of systolic blood pressure was 166 mmHg vs 120 mmHg in group A and group B respectively which was statistically significant (p value 0.000).

The mean diastolic blood pressure was 102mmHg vs 78mmHg in group A and group B respectively which was statistically significant (p value 0.000).

The mean of MAP was 124mmHg vs 92mmHg in group A and group B respectively which was statistically significant (p value 0.000).

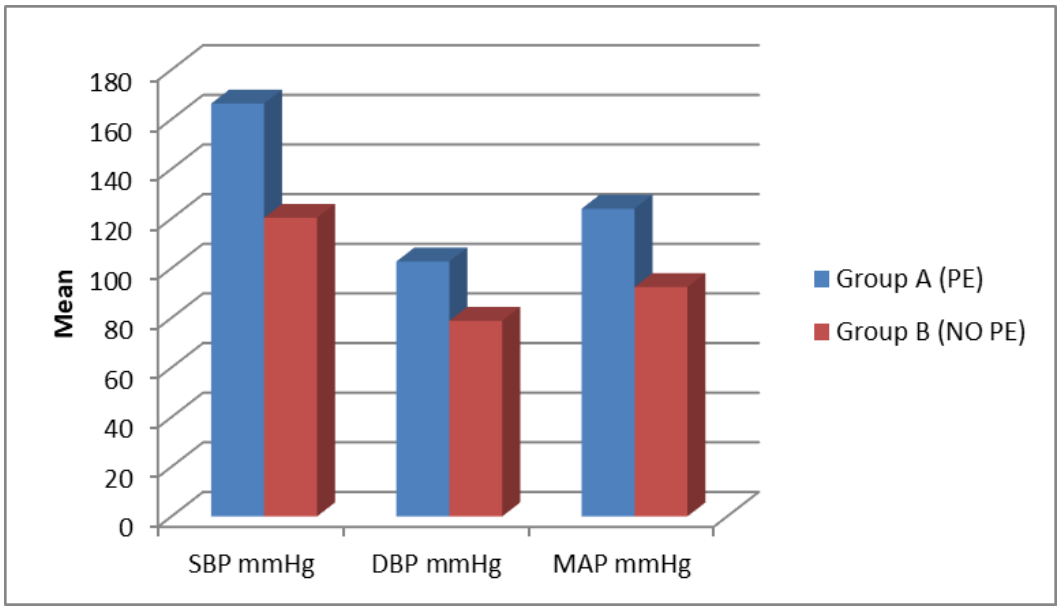

FIGURE 18: Comparison of study population of preeclampsia according to Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP).

2. Uterine Artery Doppler:

TABLE 19: Comparison of mean uterine artery Pulsatility index (PI) in preeclampsia.

Mean UtA PI	Median	IQR	Z	p-value
Group A (PE) n=11	2.02	1.83-2.2	-4.871	0.001
Group B (No PE) n=75	1.3	1.08-1.7		

The median value of mean uterine artery PI in was 2.02 vs 1.3 in group A and group B respectively which was statistically significant (p value 0.001).

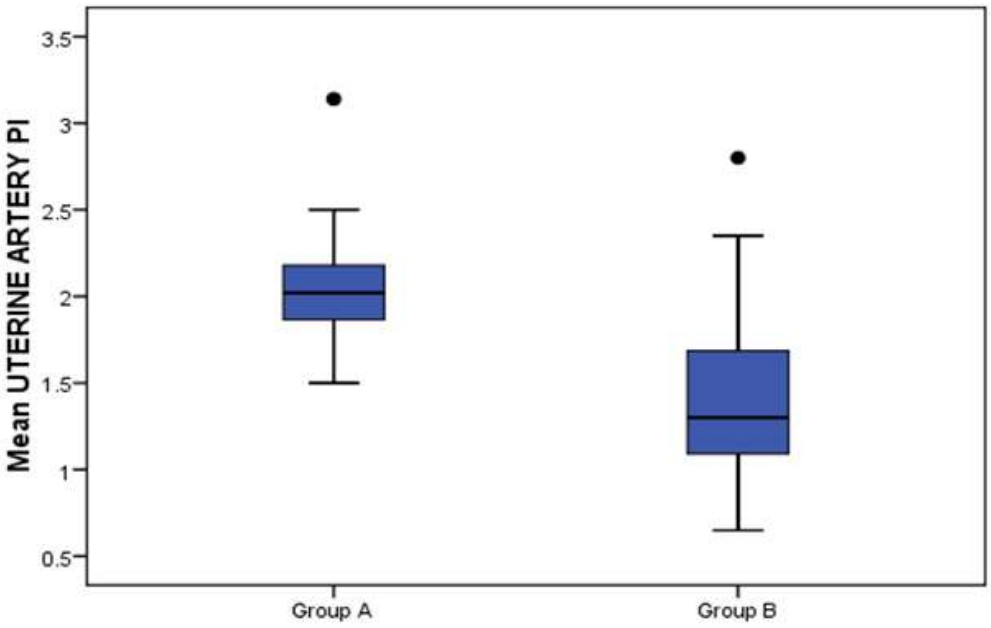

FIGURE 19: Comparison of mean uterine artery Pulsatility index (PI) in preeclampsia.

C. Biochemical parameters:

The biochemical parameters studied for first trimester prediction of preeclampsia was PlGF.

Placental Growth Factor (PlGF):

TABLE 20: Comparison of PlGF in preeclampsia.

PlGF (pg/ml)	Median	IQR	Z	p-value
Group A (PE)	30	22-32.7	-3.215	0.002
Group B (No PE)	51	39.4-71.74		

The median value of PlGF was 30pg/ml vs 51pg/ml in group A and group B respectively which was statistically significant (p value 0.002).

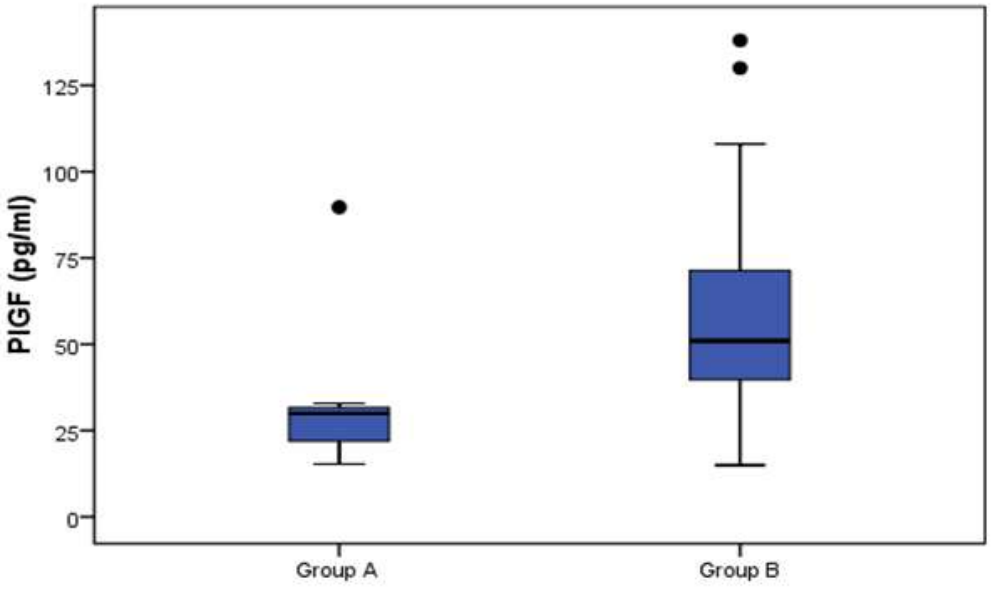

FIGURE 20: Comparison of PlGF in preeclampsia.

D. Obstetric outcome:

TABLE 21: Obstetric outcome in preeclampsia.

Obstetric outcome	Group A (PE)		Group B (No PE)		Chi-square value	p-value
	n=11	%	n=75	%		
Abortion	0	0.0%	6	8.0%	0.946	0.331
LSCS	7	63.6%	39	52.0%	0.522	0.469
MTP	0	0.0%	2	2.7%	0.303	0.584
VD	4	36.4%	27	36.0%	0.006	0.981

None of the abortions were seen in group A vs 8% in group B.

LSCS and VD were reported as 63.6% vs 52%, 36.4% vs 36% in group A and group B respectively.

None of the MTP's were seen in group A vs 2.7% group B.

All of the findings were statistically insignificant.

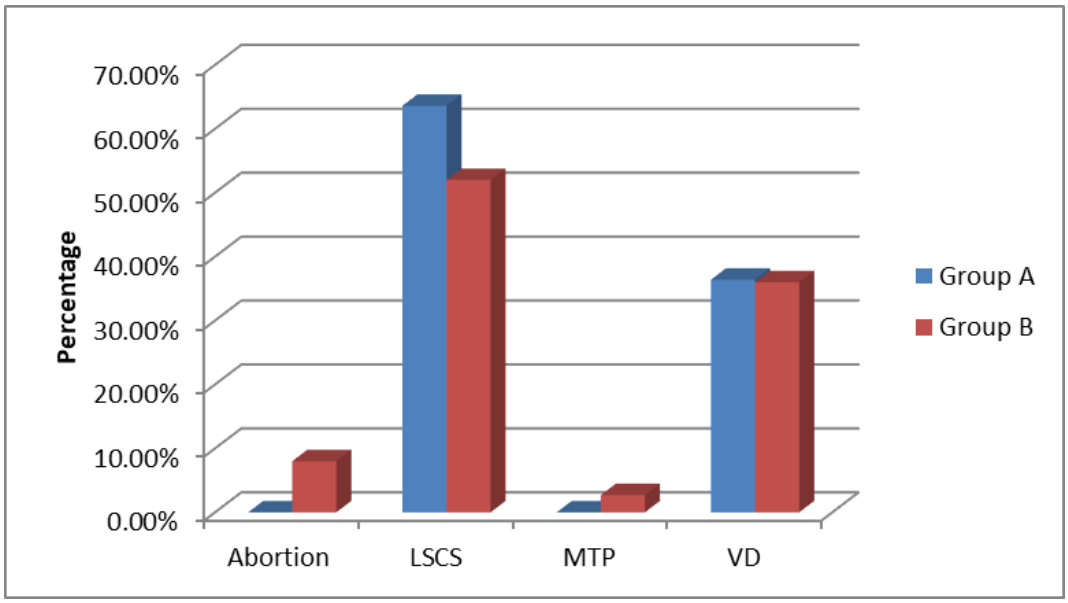

FIGURE 21: Obstetric outcome in preeclampsia.

E. Neonatal outcome:

I) Neonatal complications

TABLE 22: Comparison of NICU admissions in preeclampsia.

Neonatal outcome	Group A (PE)		Group B (No PE)		Chi-square value	p-value
	n=11	%	n=75	%		
NICU Admission	11	100.0%	9	12.0%	41.624	0.001
Neonatal death	0	0%	0	0%	0	0
Other complications	0	0%	0	0%	0	0

Of the 20 NICU admissions, 100% vs 12% were from group A and group B respectively and this was statistically significant (p value 0.001).

There were no neonatal deaths or complications in either of the groups.

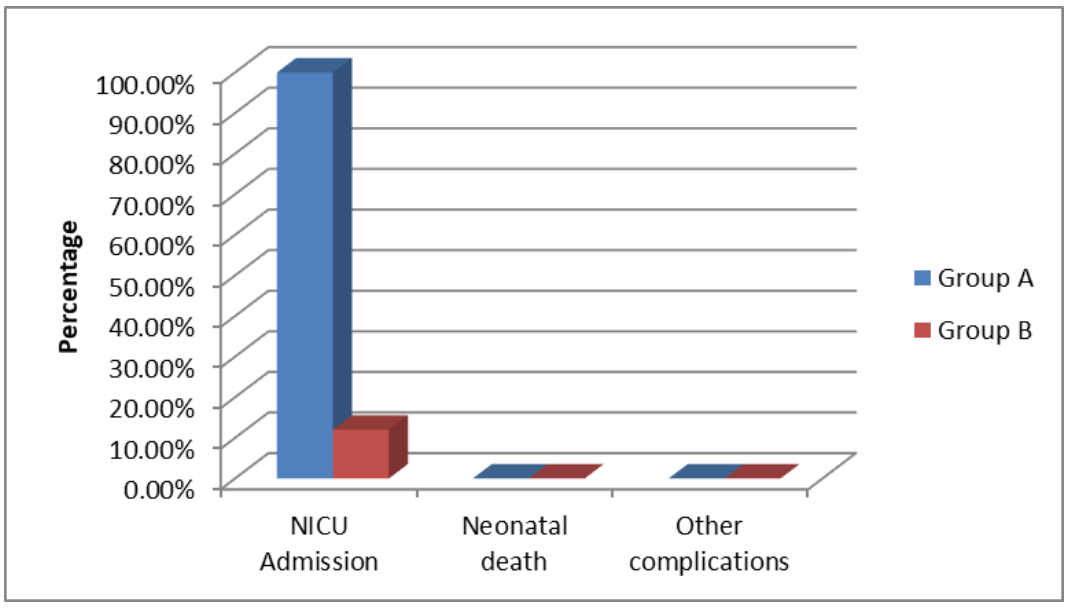

FIGURE 22: Comparison of NICU admissions in preeclampsia.

II) Neonatal Birth Weight:

TABLE 23: Distribution of neonates according to birth weight in preeclampsia and no preeclampsia group.

Birth weight	Group A (PE)		Group B (No PE)		Chi-square value	p-value
	n=11	%	n=75	%		
<1KG	2	18.2%	9	12.0%	0.328	0.566
1-1.4 KG	3	27.3%	2	2.7%	10.607	0.001
1.5-1.9 KG	2	18.2%	1	1.3%	8.088	0.004
2.-2.4 KG	2	18.2%	6	8.0%	1.178	0.277
> 2.5 KG	2	18.2%	57	76.0%	14.869	0.001

In our study, 18.2% vs 12% in group A vs group B had neonatal birth weight <1 kg which was statistically insignificant (p value 0.566).

Of the population, 27.3% vs 2.7% in group A vs group B had neonatal birth weight between 1-1.4 kg which was statistically significant (p value 0.001).

Of the population,18.2% vs 1.3% in group A and group B had neonatal birth weight between 1.5-1.9kg which was statistically significant (p value 0.004).

In the study population 18.2% vs 8% ia group had babies between 2-2.4kg which was statistically insignificant (p value 0.277).

Of the population,18.2% of preeclampsia group vs 76% of no preeclampsia group had babies with weight > 2.5 kg which was statistically significant (p value 0.001).

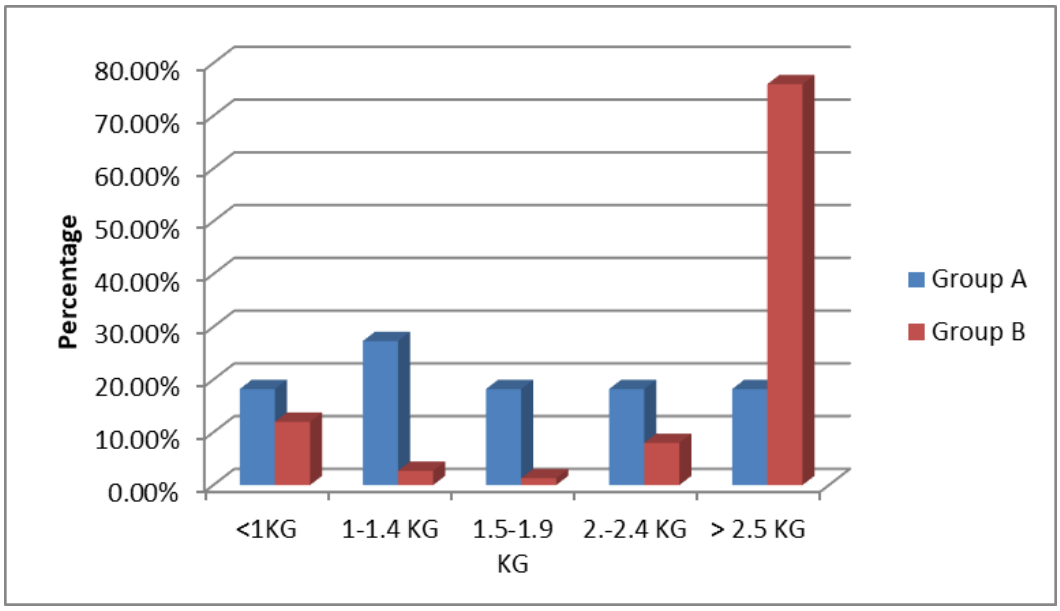

FIGURE 23: Distribution of neonates according to birth weight in preeclamptia and no preeclampsia groups.

F. Performance markers of first trimester MAP, ultrasound Ut Artery PI and PlGF individually and in combination for Preeclampsia:

TABLE 24: Performance of screening for preeclampsia.

Statistic	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
MAP	90.91	97.33	83.33	98.65	96.51
Ut PI	81.82	84	42.86	96.92	83.72
PlGF	90.91	88	52.63	98.51	88.37
MAP+ UtPI	90.91	84	45.45	98.44	84.88
MAP+ PlGF	100	88	55	100	89.53
UtPI+ PlGF	100	76	37.93	100	79.07
MAP+ UtPI+ PlGF	100	76	37.93	100	79.07

In our study the screening for preeclampsia with first trimester mean arterial pressure (MAP), had a sensitivity of 90.91%, specificity of 97.33% with positive predictive value of 83.33%, negative predictive value of 98.65% and accuracy of 96.51% respectively.

In our study the screening for preeclampsia with first trimester Uterine artery pulsitility index (UtA PI) had a sensitivity of 81.82%, specificity of 84% with positive predictive value of 42.86%, negative predictive value of 96.92% and accuracy of 83.72% respectively.

In our study the combined screening for preeclampsia with Placental growth factor (PlGF) had a sensitivity of 90.91%, specificity of 88% with

positive predictive value of 52.63%, negative predictive value of 98.51% and accuracy of 88.37% respectively.

In our study the screening for preeclampsia with first trimester mean arterial pressure (MAP) and Uterine artery pulsatility index (UtA PI) had a sensitivity of 90.91%, specificity of 84% with positive predictive value of 45.45%, negative predictive value of 98.44% and accuracy of 84.88 respectively.

In our study the screening for preeclampsia with first trimester mean arterial pressure (MAP) and Placental growth factor (PlGF) had a sensitivity of 100%, specificity of 88% with positive predictive value of 55%, negative predictive value of 100% and accuracy of 89.53% respectively.

In our study the screening for preeclampsia with first trimester Uterine artery pulsitility index (UtA PI) and Placental growth factor (PlGF) had a sensitivity of 100%, specificity of 76% with positive predictive value of 37.93%, negative predictive value of 100% and accuracy of 79.07% respectively.

In our study the combined screening for preeclampsia with first trimester mean arterial pressure (MAP), Uterine artery pulsitility index (UtA PI) and Placental growth factor (PlGF) had a sensitivity of 100%, specificity of 76% with positive predictive value of 37.93%, negative predictive value of 100% and accuracy of 79.07% respectively.

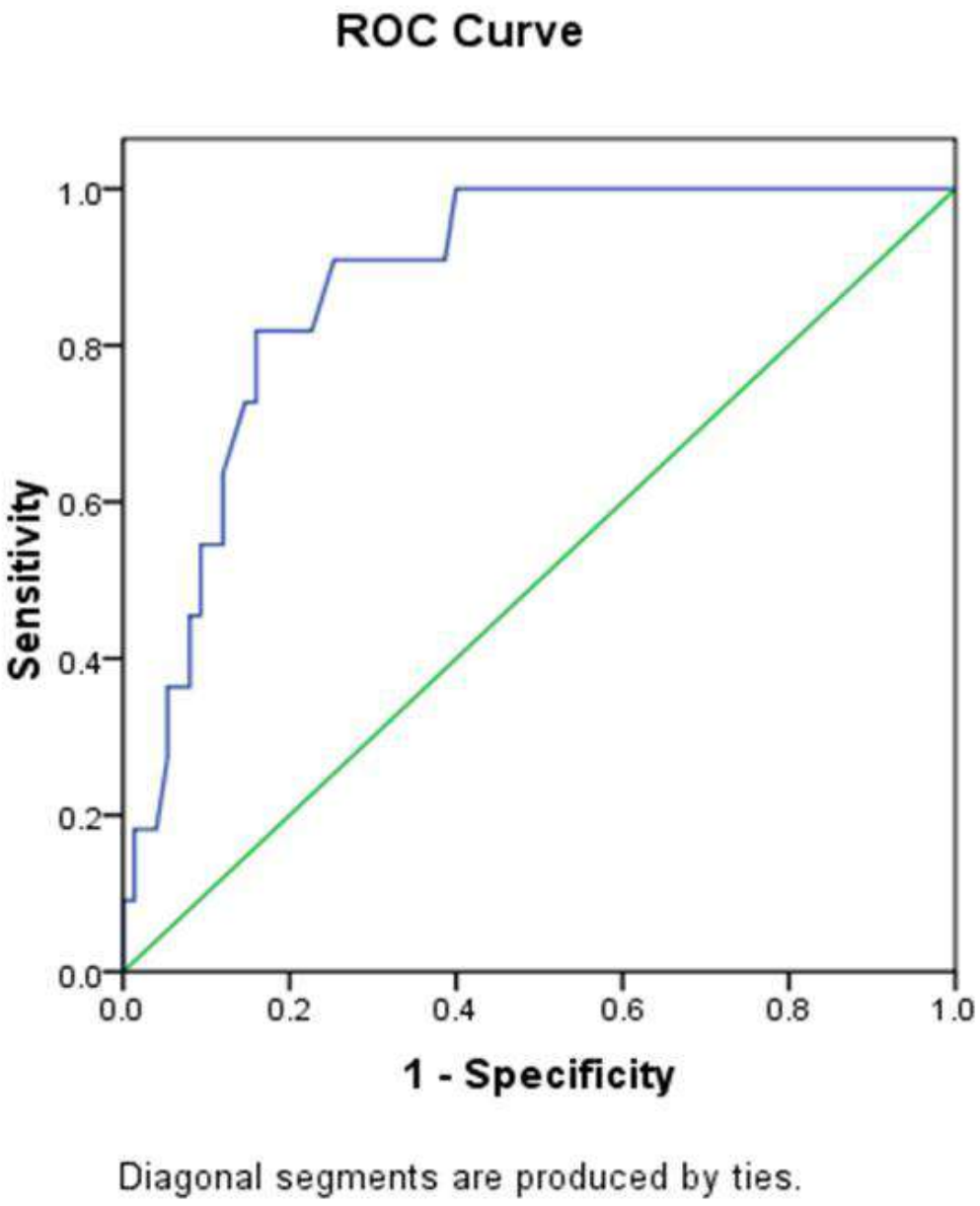

FIGURE 24: ROC of mean uterine artery PI for preeclampsia (AUC 0.879), Cutoff: < 1.8.

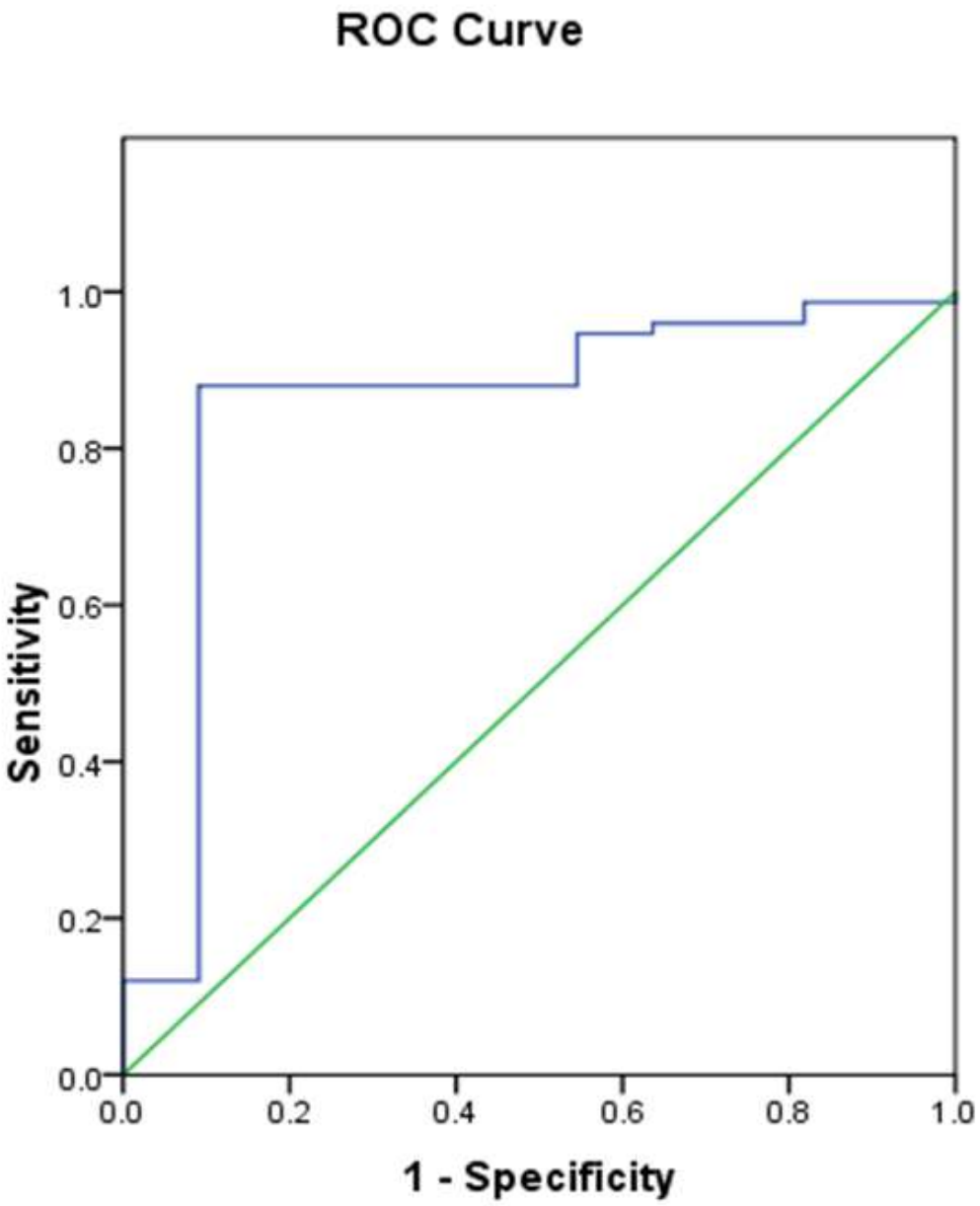

FIGURE 25: ROC curve of PlGF for preeclampsia (AUC 0.851), Cutoff: < 32.95 pg/ml.

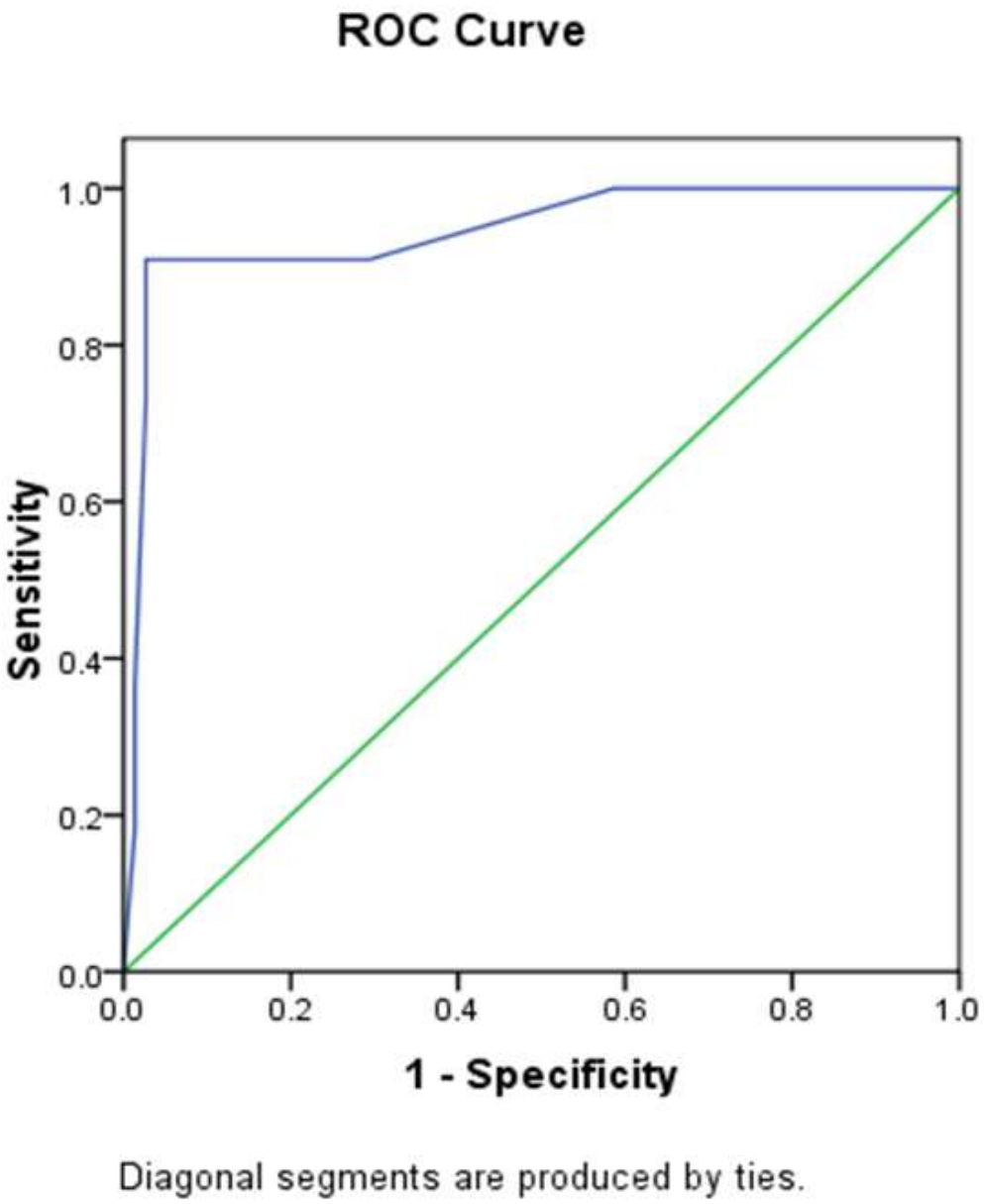

FIGURE 26: ROC curve of MAP for preeclampsia (AUC 0.944), cutoff: >115mmHg.

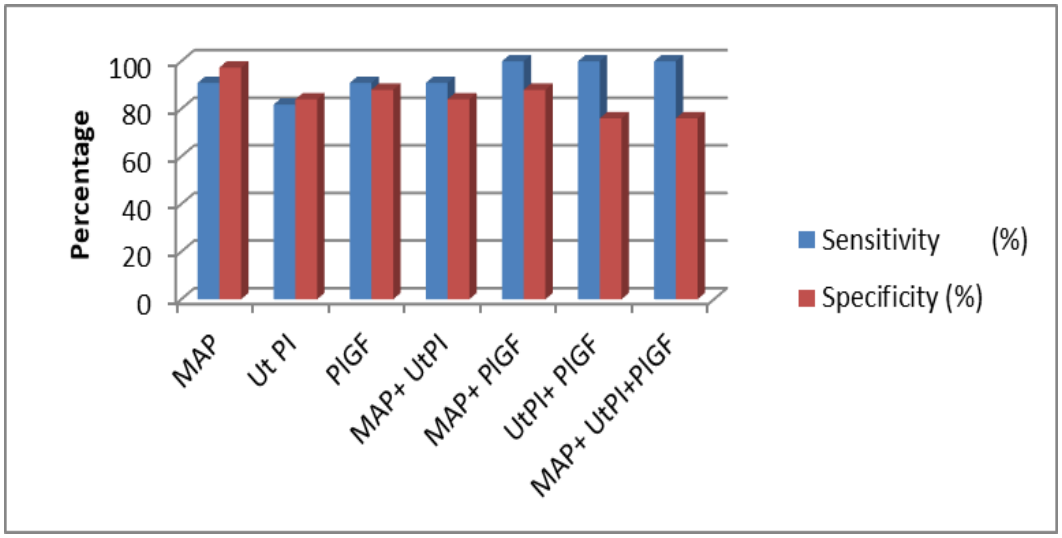

FIGURE 27: Performance markers of first trimester MAP, ultrasound Ut Artery PI and PlGF individually and in combination for Preeclampsia.

6. Prediction of aneuploidy:

The prediction includes the following components:

A. Group stratification according to first trimester screening for aneuploidy

B. Prenatal genetic testing

C. Performance of PlGF for aneuploidy

A. First trimester biochemical screening for aneuploidy

First trimester screening done was analysed as low risk(group C) and high risk (group D) and these patient specific risks were calculated by multivariate likelihood approach. The cut-off was 1:250 for trisomy 18, trisomy 21, trisomy 13. Low risk comprised group C and high risk comprised group D.

TABLE 25: Distribution of women under study according to biochemical first trimester screening.

First Trimester Screening	No. of cases	Percentage
Low Risk (Group C)	67	77.9%
High Risk (Group D)	19	22.1%
Total	86	100.0%

Of the study population, 77.9% vs 22.1% patients were from low risk and high risk groups respectively.

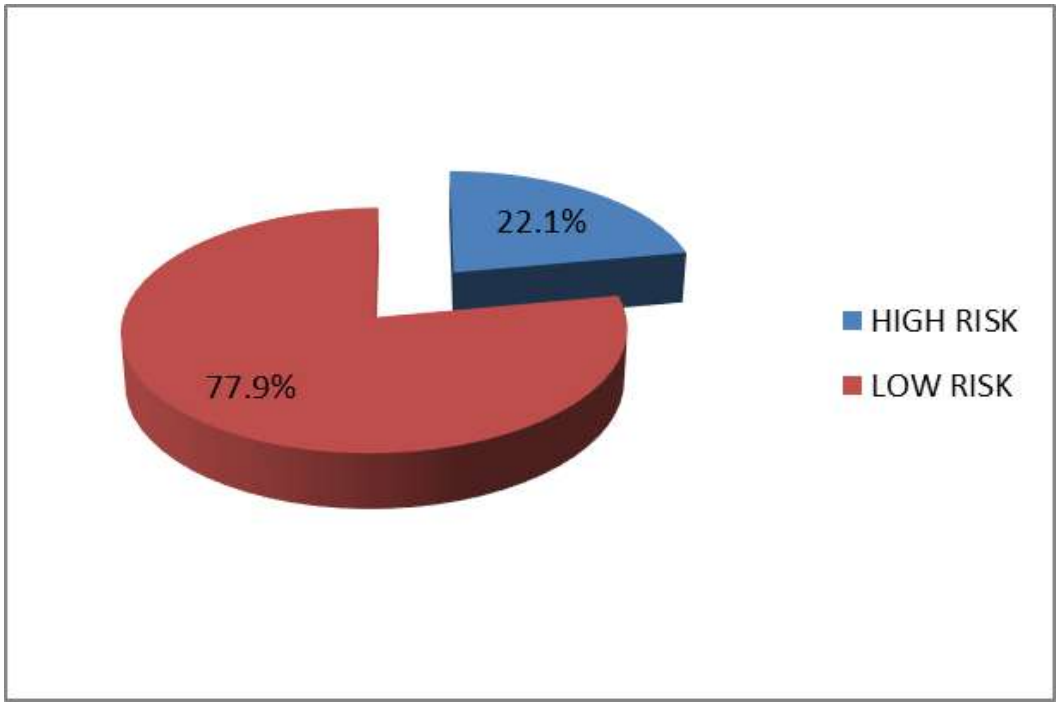

FIGURE 28: Distribution of women under study according to biochemical first trimester screening.

B. Prenatal genetic testing:

TABLE 26: Evaluation of women in high-risk group.

High risk (Group D)	No. of cases	Percentage
Amniocentesis	13	68.4%
NIPT(cffDNA)	5	26.3%
CVS	0	0%
Refused	1	5.3%
Total	19	100.0%

Out of 19 high risk patients, 68.4%, 26.3% and zero opted for amniocentesis, NIPT (noninvasive prenatal testing/ cell free fetal DNA) and CVS (Chorionic Villous Sampling) respectively. Only 1 out of 19 high risk patients refused diagnostic testing.

TABLE 27: Distribution of high risk patients according to diagnostic testing.

High Risk (Group D)	No. of cases	Percentage
Abnormal karyotype	7	36.8
Normal karyotype	12	63.2
Total	19	100

Out of 19 patients, 36.8% vs 63.2% had abnormal and normal karyotype respectively on invasive diagnostic testing.

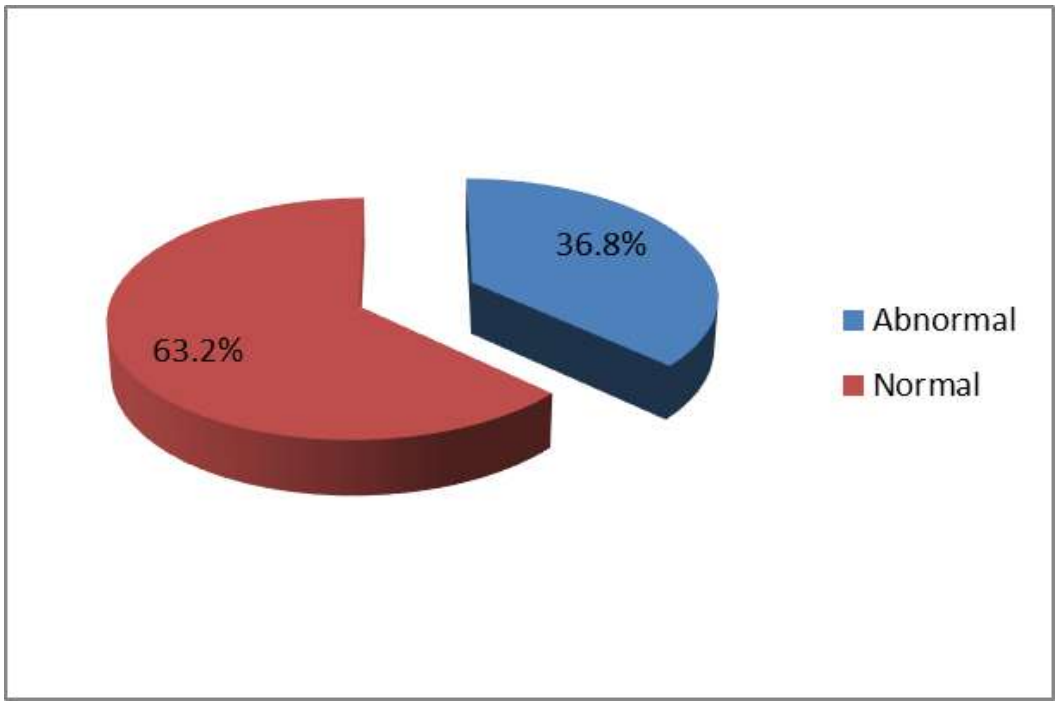

FIGURE 29: Distribution of high risk patients according to diagnostic testing.

C. Performance of PlGF for aneuploidy

TABLE 28: AUC of PlGF for aneuploidy.

PlGF	
Mean area under curve	0.708
95% CI	0.465-0.951

The mean area under curve for PlGF at a cutoff of 56 pg/ml was 0.708 at 95% confidence interval of 0.465-0.951.

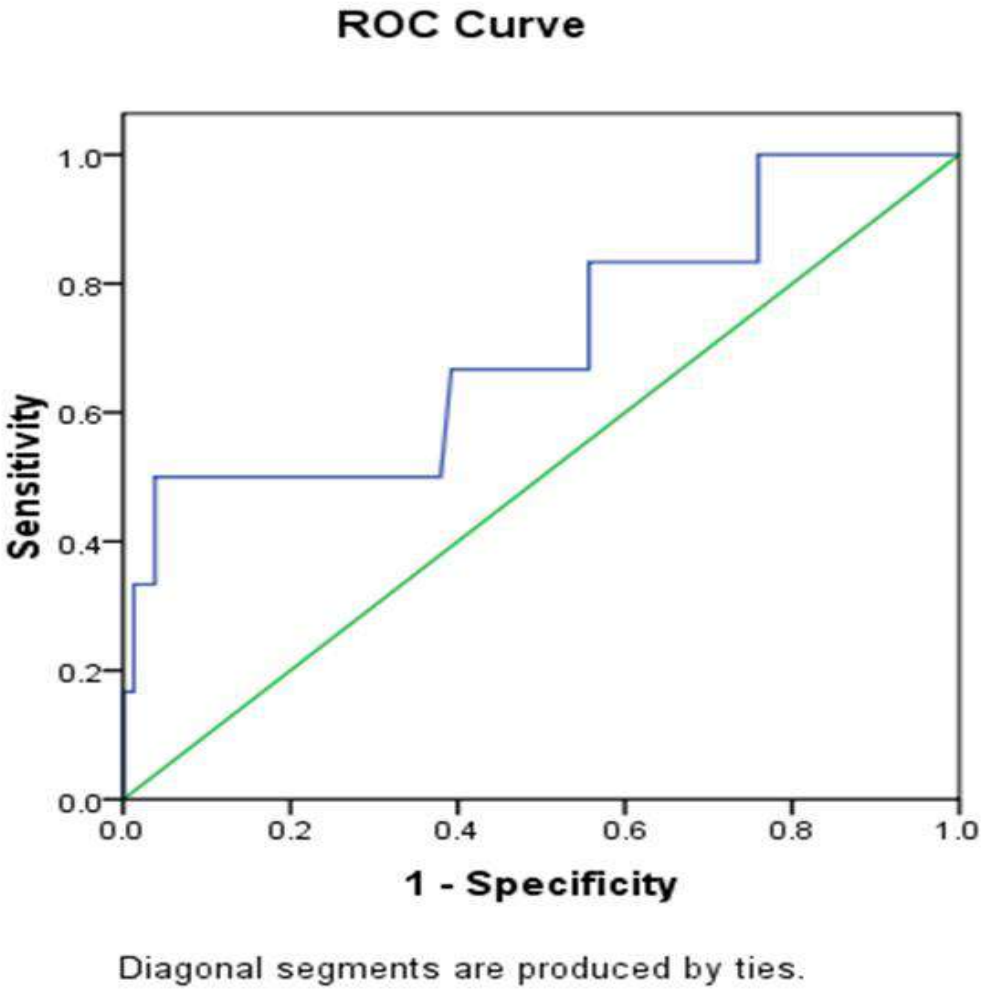

FIGURE 30: ROC of PlGF for aneuploidy cutoff: <56 pg/ml.

TABLE 29: Performance of screening for aneuploidy with first trimester biochemical screening, PlGF and both combined.

	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Accuracy %
B-hCG +PAPP-A	77.78	77.91	26.92	97.10	77.89
PlGF	50	37.97	5.77	90.91	38.82
B-hCG +PAPP-A + PlGF	100	84.81	33.3	100	85.88

The accuracy of prediction of aneuploidy with combining PlGF with β hCG and PAPP-A improved from 77.89% with β hCG and PAPP-A to 85.88% with all biochemical markers combined. PlGF alone had an accuracy of 38.82%.

The sensitivity, specificity, positive predictive value and negative predictive value of β hCG and PAPP-A combined together for aneuploidy was 77.78,77.91,26.92 and 97.10% respectively.

The sensitivity, specificity, positive predictive value and negative predictive value of PlGF for aneuploidy was 50,37.97,5.77 and 90.91% respectively.

The sensitivity, specificity, positive predictive value and negative predictive value of PlGF combined with β hCG and PAPP-A for aneuploidy was 100,84.81,33.3 and 100% respectively.

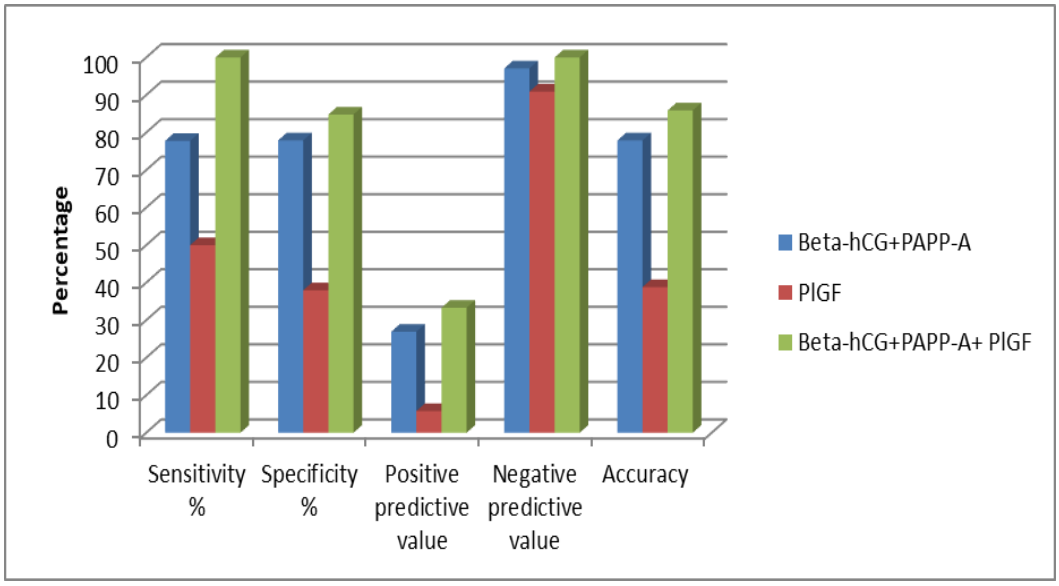

FIGURE 31: Performance of screening for aneuploidy with first trimester biochemical screening, PlGF and both combined.

DISCUSSION

This study was conducted to determine the predictive value of first trimester screening in pregnancy combined with uterine artery doppler for mean pulsatility index and placental growth factor for preeclampsia and aneuploidy.

Demography:

The mean age of the study population was 30.31 years with a standard deviation of 4.09 and the mean BMI was 25.42kg/m^2 with a standard deviation of 3.32. Our patients had pregnancy at a young age and were overweight. This is attributed to the local and geographical variations. This data is in accordance with Serra et al's 2020 study where median age was 32 years and median BMI was 23.8 kg/m^2 in singleton pregnancies for routine first trimester screening.[20]

In our study, a majority (69.7% each) of women were graduates and belonged to upper middle class. In our study population 83% women were from low-risk group in terms of obstetric history and 82% did not have an identifiable risk factor. These findings could be due to the fact that our hospital is a tertiary care center which receives educated women coming from upper socioeconomic classes.

In our study, a majority of women were multiparous (55.8%) with only 44.2% primigravida reported in DMCH for antenatal care. This may be due to the fact that primigravida were hesitant coming to tertiary referral hospital catering to complicated cases. Nagavarapu et al in 2019 reported that majority of women accessed primary and secondary facilities as a first option for birth. Further, 22.8% of the women interviewed indicated that, for their next delivery, they would prefer a government hospital closer to home. Moreover, medical expenses including medicines, travel, administrative costs as well as food and associated costs for the person/s accompanying the woman are a major reason for indebtedness among the Indian.[96]

In our study the mean gestational age at the time of screening was 12^{+3} weeks. The mean value of mean arterial pressure was 96.47mmHg with a standard deviation of 14.58.Tukk et al in 2017 suggested that in uncomplicated pregnancies, arterial blood pressure pattern usually consists of a steady decrease in blood pressure during the first half of pregnancy, then an increase until the time of delivery.[97] In our study the median value mean uterine artery pulsatility index was 1.44. There is a rise in the diameter of the uterine artery throughout pregnancy due to the increasing levels of estrogens, which have a vasodilatory effect. In our study the median value of PlGF was 47.40 pg/ml. PlGFvalue are lower in pregnancies complicated by PE and aneuploidy as compared to normal pregnancies. Similar results were reported by Serra et al in 2020. The median value of MAP was 81.04mmHg, median value of mean uterine artery pulsatility index was 1.79 and median PlGF level was 44.3 pg/ml at 12 weeks. The results are comparable to our study.[20]

Prediction of preeclampsia:

In our study of 86 patients, 11 developed preeclampsia making the disease incidence of 12.7%. Das et al in 2022 documented the incidence of preeclampsia to be 12.7% which is comparable to our study.[23] The worldwide incidence is 5-7% which may be attributed to sample size variations and geographical variations.[1-4]

The incidence of early onset preeclampsia was more than late onset preeclampsia in our study I.e. 63.6% vs 36.3%. Our hospital is a tertiary care unit with more numbers of antenatal checkup. This might be one reason for early detection and treatment of early onset preeclampsia. Li B et al in a 2022 study had similar results because the study included women reporting to a single tertiary hospital.[98] However, Serra et al in a 2020 study had more incidence of late onset preeclampsia (2%) than early onset preeclampsia (0.24%).[20] One of the reasons for higher incidence of LOPE in Serra's study could be greater sample size collected over

different centers where majority of women are diagnosed much later due to poor compliance to antenatal checkups.

In our study the mean age in preeclampsia group was 30.18 years vs 30.33 years in no preeclampsia group. The association between advanced maternal ages and adverse pregnancy outcomes has several possible explanations including the blood vessels ageing process, arterial stiffness, maternal hemodynamic adaptation impairment, lower ovum quality, obesity, unhealthy lifestyles, and comorbid disease.[99] The results were comparable to a study by Serra et al in 2020 where the median age was 34 years vs 33.9 years in preeclampsia and no preeclampsia group respectively.[20] The results in our study involving maternal age show no association with preeclampsia in any age group. Our results were in accordance with the study by Salem et al in 2018. There was no significant difference between preeclampsia and no preeclampsia group with regards to maternal age in their study.[27]

In our study the mean BMI in preeclampsia group 25.47 kg/m^2 vs 25.41 kg/m^2 in no preeclampsia group. Majority of the patients in both the groups were overweight and p value was not significant. The dominating overweight population could be due to local variations and better lifestyle options in our study population. Our results were in accordance with the studies by Salem et al in 2018. There was no significant difference between preeclampsia and no preeclampsia group with regards to BMI in this study. Salem et al reported that the mean BMI was 24.1 kg/m2 vs 23.7 kg/m2 in preeclampsia vs no preeclampsia group.[27] In a cohort study by Wei M et al in 2015 higher pre-pregnancy BMI is associated with higher prevalence of preeclampsia[100] because obesity is known as a state of chronic, low-grade inflammation, also called “meta-inflammation". Low-grade inflammation can induce endothelial dysfunction and placental ischemia by immune-mediated mechanisms, which in turn lead to production of inflammatory mediators resulting in an exaggerated maternal inflammatory response and development of PE.

In a Chhattisgarh based study by Das et al in 2022, it was observed that age and BMI in preeclampsia and no preeclampsia groups were not significant.[23] These demographic differences were probably due to the study being set in a single tertiary care center. Increased study duration with a greater sample size involving two or more centers located in different areas may have given better results.

Risk factors:

In our study nulliparous women were indeed more prone to having preeclampsia as compared to multiparous ones (p value: 0.054). Nulliparous women who are exposed to placenta for the first time are characterized by a relatively antiangiogenic state. This may be a potential molecular mechanism that explains the link between preeclampsia and nulliparity. In a study by Bdolah Y et al in 2014 nulliparous pregnancies had higher circulating sFlt1 levels and sFlt1/PlGF ratios than multiparous pregnancies, suggesting an association with an angiogenic imbalance.[101]

In our study previous preeclampsia was seen in 18.2% vs none in preeclampsia and no preeclampsiagroup respectively. Women with previous preeclampsia were significantly at a higher risk of developing preeclampsia in current pregnancy (p value 0.001). This is in accordance with the study by Brouwer's et al in 2018 which reported that in 15% of women, pre-eclampsia recurs in the following pregnancy.[102]

Biophysical parameters

In our study the mean arterial pressure (MAP) was significantly higher (p value 0.000) in the preeclampsia group (124mmHg) than the unaffected group (92.43mmHg) after 20 weeks of pregnancy. This could be due to the fact that in our study population a majority of the patients had risk factors like advancing age, obesity, previous preeclampsia and nulliparity. ACOG in 2020 reported all of these as important risk factors for preeclampsia.[26] In a study by Tzur et al in 2021 it was reported that women who subsequently developed preeclampsia with severe features had higher proteinuria levels at diagnosis.[103] The cutoff in our study was

found to be 115mmHg (as obtained from ROC curve). Gallo d et al in 2014 reported that in pregnancies that develop preeclampsia, mean arterial pressure at 20–24 weeks' gestation is higher than in normal pregnancies.[104] Galo et al reported the median value of MAP was 91.7 mmHg vs 83.9 mmHg in preeclampsia and no preeclampsia group respectively with a p value of <0.0001. He concluded that performance of screening for PE by MAP is best when measurements are taken at both 11-13 and 20-24 weeks gestation.[104]

The mean uterine artery PI value among those who developed preeclampsia was 2.02 and was significantly higher than the unaffected group i.e. 1.3 (p value 0.001). This supports the theory of abnormal placentation, a characterstic pathophysiology of preeclampsia leading onto increased vascular resistance in placenta. The ultrasonographic evidence of this problem is seen as an increase in pulsatility index (PI) of the uterine artery.[27] Similar results were seen in studies by Elkholi et al in 2016, Serra et al in 2020 and Das et al in 2022 where the mean PI in preeclampsia group was 2.66, 2.1 and 2.007 respectively.[105][20][23] The cutoff in our study was found to be 1.82 (as obtained from ROC curve). A similar cutoff was also found by Salem et al (1.69).[27]

Biochemical parameters:

The median value of PlGF was 30pg/ml in the preeclampsia group which was significantly lower than the unaffected group where the median value was 51 pg/ml (p value: 0.002). There is a link between maternal underperfusion and an anti-angiogenic state characterized by the changes in the concentrations of angiogenic and anti-angiogenic factors in women with preeclampsia.The limited production of PlGF in placental tissue allowed it to be used as a predictive marker for preeclampsia.This is in accordance with study by Serra et al where median PlGF was 19.5 pg/ml and 26.5 pg/ml in early onset and late onset preeclampsia respectively.[20] The cutoff in our study was found to be 32.95pg/ml (as obtained from ROC curve). In a metanalysis of 40 studies by Agrawal et al in 2019 the

optimal cutoff values were given as a discrete number, which was between 41 and 382 pg/mL or in multiples of median. The results emphasize the need for a standardized cutoff and warrant further trials to explore the levels of PlGF. The gestational age and population specific threshold might also affect the predictive capacity of PlGF.[59]

Obstetric and neonatal outcome:

Of the preeclampsia group 63.6% vs 36.4% had cesarean vs normal delivery and in the no preeclampsia group 52% vs 36% had cesarean vs normal delivery respectively. Early detection and timely management of preeclampsia was done in our center and so the mode of delivery was comparable in both the groups. There were no maternal adverse events that required immediate delivery. This was in accordance with study by Venkatesh KK et al in a 2020 retrospective study where preeclampsia with severe features <34 weeks complicated by comorbidity was generally not associated with an increased risk of adverse maternal outcomes.[106]

The preeclampsia group had higher number of NICU admissions than the no preeclampsia group and this was statistically significant. Growing body of evidence indicates that neonates born to preeclamptic patients are physiologically immature compared to infants born at term and are at significant risk for a wide range of complications because of associated neonatal morbidity and mortality. These findings were in accordance to a systematic review in 2022 by Atamamen et al. where prematurity and fetal growth restriction were most common patterns in these NICU admissions.[107][108]

The preeclampsia group had maximum neonates with birth weight between 1-1.4 kg and 1.5-1.9 kg as compared to no preeclampsia group (p value 0.001 and 0.004 respectively) which was statistically significant. Lower birth weight is more likely a reflection of the effect of preeclampsia on placental function and fetal growth rather than that of prematurity alone. This was comparable to a retrospective study in 2020 by Mckenzie

et al where neonates born to women with preeclampsia were more likely to be low birth weight, small for gestational age or premature.[109]

Performance of screening for preeclampsia:

In our study, PlGF levels had a sensitivity of 90.91% and accuracy of 88.37% for predicting preeclampsia. Salem et al in 2018 used PlGF to predict preeclampsia and reported a sensitivity of 90% and accuracy of 83%.[27] This suggests that PlGF is a feasible tool to predict preeclampsia.

The mean uterine artery pulsatility index in our study had a sensitivity of 81.82% and accuracy of 83.72% in predicting preeclampsia.In a 2020 study by Oancea et al, based on pulsatility index analysis, doppler examination of the uterine artery performed early at 11-13 $^{+6}$ weeks allows the detection of pregnancies that will develop PE with a sensitivity of 61.5% and a specificity of 63.8%.[12] In a study by Das et al in 2022 the first-trimester uterine artery PI as a screening tool had a sensitivity of 68%, specificity of 52.99%, positive predictive value (PPV) of 23.61%, negative predictive value (NPV) of 88.57%, and a detection rate (DR) of 55.63%.[23] Hence, Uterine artery Doppler examination is an effective non-invasive screening test for the development of PE in pregnancies at risk, particularly appropriate in health systems with limited means of evaluating other biomarkers.

In our study the combination of uterine artery pulsatility index and placental growth factor had a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of i.e. 100%, 76%, 37.93%, 100% and 79.07% respectively. Similar findings were reported for this combination by Elkholi et al in 2016 where the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 92.85%, 87.6%, 28.88%, 99.54% and 87.59% respectively.[105] Thus, the ideal first trimester markers for prediction of preeclampsia may be a combination of UtA-PI and maternal serum PlGF.

The combination of mean arterial pressure, mean uterine artery pulsatility index and placental growth factor had a sensitivity of 100%, specificity of

76% with positive predictive value of 37.93%, negative predictive value of 100% and accuracy of 79.07%. In 2020 Serra et al used an algorithm by fetal medicine foundation combining MAP, UtA-PI and PlGF and reported a detection rate of 94.1% at a false positive rate of 10%.[20] O'Gorman N et al in 2017 used the same combination to give a detection rate of 100% at a 10% false positive rate.[110] Due to heterogenous nature of preeclampsia, prediction cannot not be achieved by a single test. In our study, no single marker has a satisfactory predictive value in preeclampsia, however, they are more beneficial when combined together.

Prediction of aneuploidy:

Out of 86 patients, 19 (22.1%) were at high risk for aneuploidy according to first trimester biochemical screening. In a study done by Anita kaul et al in 2016 , 2.8% patients were at high risk of aneuploidy. This disparity of the results may be attributed to sample size and geographical variations.[111]

In our study a majority (77.9%) of population was screen negative as the mean age of the population was 30 years and there was no history of any genetic disorders. In a study in 2019 El-Attar et al reported that advanced maternal age could be considered as possible risk factor for Down syndrome.[112]

In our study out of the high risk group, only 36.8% (7 out of 19) had an abnormal karyotype on prenatal genetic testing. This implies that a majority of high risk group patients had a normal karyotype with prenatal genetic testing because according to Cochrane database 0f 2015, prenatal genetic testing has an accuracy of nearly 98-99%%. Since, combined first trimester biochemical screening has a detection rate of 73% it explains higher percentage of our study population under highrisk group of aneuploidy.[88] In a 2017 cochrane database by Badeau et al, it was concluded that invasive fetal karyotyping is still the required diagnostic approach to confirm the presence of a chromosomal

abnormality prior to making irreversible decisions relative to the pregnancy outcome.[113]

Performance of screening for aneuploidy:

The incidence of aneuploidy was 8.1% in our study. On adding placental growth factor to the routine first trimester biochemical testing for predicting aneuploidy improved the accuracy from 77.89% to 85.88%. Boudin et al in 2018 reported that a combination of nuchal translucency, maternal age and PlGF had a detection rate of 92%.[114] In a study by Pandya et al in 2012 the combination of β hCG, PAPP-A and PlGF had a detection rate of 84% at 10% false positive rate.[115] So, inclusion of PlGF when screening for trisomies has shown to improve first trimester screening for aneuploidies.

To predict aneuploidy, PlGF levels in our study were either increased (cutoff: 56pg/ml) or not significantly different from normal cutoff values. This was probably because these values did not adjust the measured values for maternal variables and different age of gestation at the time of screening. Moreover, the levels were done in different laboratories of the city which might have been a reason for biased results.

According to a Cochrane database from 2022, preeclampsia is a condition which lends itself to screening. It is justified for the following reasons:

- Opportunity for prevention through targeted prophylaxis.
- Allow early risk stratification and triage into high-risk care.
- Increased maternal and fetal surveillance. It is known that a delay in diagnosis of preeclampsia can contribute to maternal morbidity and mortality.
- Identification of a population in which trials of novel prophylactic and/or treatment therapies can be performed.[116]

According to FMF, a multivariate gaussian distribution model including maternal factors, early PlGF determination and biophysical variables (MAP and UtA-PI) at 11 weeks to 13 $^{+6}$ weeks is a feasible tool for preeclampsia screening in routine care setting.[20]

Adding uterine artery doppler and placental growth factor to the routine nuchal translucency scan and first trimester screening (β human chorionic gonadotrophin and pregnancy associated plasma protein-A) from 11weeks to 13^{+6} weeks can improve the detection rates for preeclampsia as well as aneuploidy simultaneously. This combination strategy will be cost effective and it will allow a timely intervention to prevent adverse comes.

SUMMARY AND CONCLUSION

In this prospective study conducted from March 2021 to March 2022, a total of 90 patients at 11wks to 13^{+6}wks were recruited for first trimester screening combined with uterine artery doppler for pulsatility index and PlGF to predict preeclampsia and aneuploidy.

- Out of 90, 4 patients were lost to follow up, and this resulted in a data of 86 patients.
- The mean age of the study population was 30.31 years with a standard deviation of 4.09 and the mean BMI was 25.42kg/m^2 with a standard deviation of 3.32.
- A majority (69.7% each) of women were graduates and belonged to upper middle class.
- The mean gestational age at the time of screening was 12^{+3} weeks.
- The mean arterial pressure was 96.47mmHg with a standard deviation of 14.58.
- The mean uterine artery pulsatility index was 1.44.
- The median β-hCG, PAPP-A and PlGF was 0.98 MoM, 0.88 MoM and 47.40 pg/ml respectively.
- The incidence of preeclampsia was 12.7%.The incidence of early onset preeclampsia and late onset preeclampsia was 63.6% vs 36.3% respectively.
- The mean age in preeclampsia group was 30.18 years vs 30.33 years in no preeclampsia group which was statistically not significant.
- The mean BMI in preeclampsia group 25.47 kg/m^2 vs 25.41 kg/m^2 in no preeclampsia group. Majority of the patients in both the groups were overweight and result was not statistically significant.
- Nulliparous women and women with previous preeclampsia were at a higher risk of developing preeclampsia in current pregnancy. The results were statistically significant.

- The mean arterial pressure (MAP) was significantly higher in the preeclampsia group (124mmHg) than the no preeclampsia group (92.43mmHg) after 20 weeks of pregnancy.
- The mean uterine artery PI value among those who developed preeclampsia was 2.02 and was higher than the no preeclampsia group i.e. 1.3. This was statistically significant.
- The median value of PlGF was 30pg/ml in the preeclampsia group which was lower than the no preeclampsia group where the median value was 51pg/ml. This was statistically significant.
- The mode of delivery was comparable in preeclampsia and no preeclampsia groups.
- The preeclampsia group had higher number of NICU admissions and majority of neonates had low birth weight than the no preeclampsia group and this was statistically significant.
- PlGF levels had a sensitivity of 90.91% and accuracy of 88.37% for predicting preeclampsia.
- The mean uterine artery pulsatility index had a sensitivity of 81.82% and accuracy of 83.72% in predicting preeclampsia.
- The combination of uterine artery pulsatility index and placental growth factor had a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of i.e. 100%, 76%, 37.93%, 100% and 79.07% respectively in predicting preeclampsia.
- The combination of mean arterial pressure, mean uterine artery pulsatility index and placental growth factor had a sensitivity of 100%, specificity of 76% with positive predictive value of 37.93%, negative predictive value of 100% and accuracy of 79.07% in predicting preeclampsia.
- Out of 86 patients, 19 (22.1%) were at high risk for aneuploidy according to first trimester biochemical screening and 36.8% (7 out of 19) had an abnormal karyotype on prenatal genetic testing.
- The incidence of aneuploidy was 8.1%.

- On adding placental growth factor to the routine first trimester biochemical testing for predicting aneuploidy improved the accuracy from 77.89% to 85.88%.
- The limitation of this study was a small sample size and study being confined to a single tertiary centre. The results did not have a standard cut off value for PlGF because the values were not adjusted for maternal variables and different age of gestation at the time of screening. Moreover, the samples were collected from different laboratories. This might be a reason for biased results. Based on all the observations, analyses and inferences it has been observed that adding uterine artery doppler and placental growth factor to the routine nuchal translucency scan and first trimester screening (β human chorionic gonadotrophin and pregnancy associated plasma protein-A) from 11weeks to 13^{+6} weeks can improve the detection rates for preeclampsia as well as aneuploidy. This combination strategy will be a feasible tool and will allow a timely intervention to prevent adverse maternal and fetal outcomes.

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S.NO	MRD NO	NAME	AGE	BMI	LMP	SBP	DBP	MAP	EDD	ETHNICITY	SOCIO ECONOMIC STATUS	EDUCATION	MENSTRUAL HISTORY	OBS HISTORY	NEONATAL DEATH	COMORBIDITIES		PREVIOUS PE	PREVIOUS PRETERM
1	134108	NK	26	22	14/11/2020	150	100	117	21/08/2202	ASIANTIC	LOWER	GRADUATE	3D/30D	PRIMI	NO	NO		NO	NO
2	135621	SK	30	28.9	12/06/2020	160	110	127	19/03/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/28D	PRIMI	NO	NO	-	NO	NO
3	807729	AB	31	30.4	19/11/2020	120	80	93	27/08/2021	ASIANTIC	UPPER	GRADUATE	3D/28D	PRIMI	NO	NO	-	NO	NO
4	112496	KT	25	24.5	13/11/2020	120	80	93	20/08/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3-4D/28D	PRIMI	NO	NO	-	NO	NO
5	113307	VM	33	23	19/10/2020	110	70	83	26/07/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/30D	G5P1L1A3	NO	NO	NO	NO	NO
6	130841	N	34	32.7	08/12/2020	140	90	107	14/09/2021	ASIANTIC	LOWER MIDDLE	GRADUATE	3D/28D	PRIMI	NO	NO	-	NO	NO
7	123086	AA	25	28.2	02/11/2020	180	110	133	09/08/2021	ASIANTIC	UPPER	POSTGRADUATE	5D/30D	PRIMI	NO	NO	-	NO	NO
8	149962	D	36	17.5	30/12/2020	120	80	93	06/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/30D	PRIMI	NO	NO	-	NO	NO
9	595120	SS	28	22	28/12/2020	130	90	103	04/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	G2P1L1	NO	NO	NO	NO	NO
10	184712	A	25	16.1	03/01/2021	120	80	93	10/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/29D	PRIMI	NO	GDMA1	-	NO	NO
11	105336	SM	31	26.1	01/01/2021	120	80	93	08/10/2021	ASIANTIC	UPPER	GRADUATE	3D/28D	G2P1L1	NO	NO	NO	NO	NO
12	959050	GM	29	22	13/01/2021	120	86	97	19/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	2D/27D	G2P1L1	NO	ICP	NO	NO	NO
13	106699	SG	28	17.8	05/01/2021	110	70	83	12/10/2021	ASIANTIC	LOWER MIDDLE	GRADUATE	3D/28D	G2P1L1	NO	NO	NO	NO	NO
14	119162	GK	28	21.8	24/11/2020	124	82	96	31/09/2021	ASIANTIC	UPPER LOWER	GRADUATE	4D/30D	G2P1L1	NO	NO	NO	NO	PRETERM
15	109893	MS	37	24.9	01/01/2021	122	84	97	08/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/28D	G3P1L1A1	NO	NO	NO	NO	NO
16	107089	BJ	26	32	10/10/2021	130	86	101	17/10/2021	ASIANTIC	UPPER MIDDLE	POSTGRADUATE	3D/30D	G2P1L1	NO	NO	NO	NO	NO
17	128608	AJ	27	25.5	15/01/2021	126	94	105	22/10/2021	ASIANTIC	LOWER	HIGHER SECONDARY	4D/30D	PRIMI	NO	NO	-	NO	NO
18	119165	MK	24	26.1	18/01/2021	110	70	83	25/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/28D	PRIMI	NO	NO	-	NO	NO
19	109021	SK	27	28	18/07/2020	120	70	87	24/05/2021	ASIANTIC	UPPER MIDDLE	SECONDARY	4D/28D	PRIMI	NO	GDMA1	-	NO	NO
20	109814	LK	24	21	09/01/2021	110	80	90	16/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	PRIMI	NO	HYPOTHYROID	-	NO	NO
21	407643	ND	35	27.1	16/01/2021	110	70	83	23/10/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/28D	G2P1L1	NO	NO	NO	NO	NO
22	8076	SK	32	22	22/01/2021	120	70	87	29/10/2021	ASIANTIC	UPPER	GRADUATE	3D/28D	G2P1L1	NO	THALLASEMIA MINOR	THALLASEMIA MINOR	NO	NO
23	136012	MK	34	27.8	06/10/2020	170	110	130	13/07/2021	ASIANTIC	LOWER MIDDLE	HIGHER SECONDARY	5D/30D	PRIMI	NO	NO	-	NO	NO
24	109491	AS	30	25	30/01/2021	180	100	127	06/11/2021	ASIANTIC	UPPER MIDDLE	POSTGRADUATE	3D/30D	G2A1	NO	NO	NO	Y	NO
25	138044	NS	27	23.2	03/02/2021	200	100	133	10/11/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	PRIMI	NO	HYPOTHYROID	-	NO	NO
26	72798	KK	33	23	10/02/2021	-	-	-	-	-			-	-	-	-	-	NO	-
27	110892	D	36	25	14/02/2021	128	88	101	21/11/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/30D	G3P2L2	NO	HYPOTHYROID	NO	NO	NO
28	196801	S	26	28.7	12/02/2021	135	78	97	19/11/2021	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	4D/30D	PRIMI	NO	NO	-	NO	NO
29	121260	RM	30	26.5	19/02/2021	120	80	93	26/11/2021	ASIANTIC	UPPER	POSTGRADUATE	2D/28D	G3P1L1A1	NO	NO	NO	NO	PRETERM
30	111096	MJ	26	17.5	12/03/2021	120	86	97	19/12/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	PRIMI	NO	NO	-	NO	NO
31	108961	K	28	26.1	15/02/2021	110	70	83	22/11/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/30D	PRIMI	NO	NO	-	NO	NO
32	6482	HK	33	22.7	04/03/2021	120	80	93	09/12/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/30D	G2P1L1A1	NO	SLE	NO	NO	PRETERM
33	198102	HS	31	24.2	06/03/2021	126	86	99	13/12/2021	ASIANTIC	UPPER	SECONDARY	4D/30D	G2P1L1	NO	HYPOTHYROID	NO	NO	NO
34	109380	HK	28	25.4	03/03/2021	-	-	-	-	-			-	-	-	-	-	NO	-
35	108912	SM	28	24.2	01/03/2021	110	70	83	08/12/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/30D	PRIMI	NO	NO	-	NO	NO
36	66227	RA	30	24.2	05/03/2021	120	80	93	12/12/2021	ASIANTIC	UPPER MIDDLE	POSTGRDUATE	3D/28D	G2P1L1	NO	NO	NO	NO	NO
37	120475	SG	28	33.6	03/02/2021	120	80	93	10/11/2021	ASIANTIC	UPPER	HIGHER SECONDARY	4D/31D	PRIMI	NO	NO	-	NO	NO
38	109628	MR	29	25.4	10/03/2021	110	70	83	10/03/2021	ASIANTIC	LOWER MIDDLE	POSTGRADUATE	5D/30D	PRIMI	NO	NO	-	NO	NO
39	103160	PK	30	24.4	20/12/2020	110	70	83	26/09/2021	ASIANTIC	LOWER	GRADUATE	5D/28D	G5P1L1A3	NO	NO	NO	NO	NO
40	901321	A	32	25.2	14/03/2021	120	80	93	21/12/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	G3P1L1A1	NO	NO	NO	NO	NO
41	121880	C	29	32.5	11/03/2021	110	70	83	18/12/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/28D	PRIMI	NO	NO	-	NO	NO
42	109864	TK	39	28.1	11/03/2021	110	70	83	18/12/2021	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	4D/29D	G2P1L1	NO	NO	NO	NO	PRETERM
43	628867	VN	35	26.6	07/02/2021	120	80	93	14/11/2021	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/30D	G4P2L1A1	NO	NO	NO	NO	NO
44	102234	SD	24	27	28/02/2021	-	-	-	-	-		GRADUATE	-	-	-	-	-	NO	-
45	102244	D	25	24.2	10/04/2021	120	80	93	17/01/2022	ASIANTIC	UPPER MIDDLE	SECONDARY	3D/30D	G2A1	NO	NO	NO	NO	NO
46	109681	N	42	25.8	22/06/2021	112	78	89	29/03/2022	ASIANTIC	UPPER LOWER	GRADUATE	3D/40D	PRIMI	NO	THALLASEMIA MINOR	-	NO	NO
47	525644	MR	30	24	16/05/2021	110	70	83	23/02/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/35D	G2P1L1	NO	NO	NO	NO	NO

S.NO	MRD NO	ABORTIONS	TUBERCULOSIS	MULTIPLE PREGNANCIES	DIABETES	CHROMOSOMAL ABORMALITIES	CONSANGUINOUS MARRIAGE	PREMATURITY	FIRST TRIMESTER SCREENING	FAMILY HISTORY GENETIC DISORDER	FREE BETA-hCG (MoM)	PAPP-A (MoM)	PIGF (pg/ml)	HB	URINE ROUTINE	RBS	TSH	HbA2/HPLC	OGTT
1	134108	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.58	1.21	30.64	10	N	90	2.1	N	N
2	135621	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.36	1.072	89.7	10	PRO 3+	94	1.8	N	N
3	807729	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.44	0.75	43.96	12.6	N	86	3.12	N	N
4	112496	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.834	0.74	19.8	12	PRO 1+	98	2.1	N	N
5	113307	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.8	0.38	29.78	10.4	N	102	1.18	N	N
6	130841	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.44	0.34	25.57	11.2	N	106	2	N	N
7	123086	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.669	0.203	15.3	12	PRO 3+	104	1.6	N	N
8	149962	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.1	1.01	51.63	13.6	N	74	2.34	N	N
9	595120	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.39	1.12	37.67	9.7	N	106	1.21	N	N
10	184712	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.2	0.24	43.72	11.4	N	86	2.13	N	143
11	105336	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.74	1.36	71.04	11.6	N	102	2.1	N	N
12	959050	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.39	1.12	68	12	N	97	2.2	N	N
13	106699	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.16	0.47	22.5	11	N	89	1.7	N	N
14	119162	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	0.59	0.13	74.4	12	N	98	4.3	N	N
15	109893	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.55	0.88	84.63	12	N	96	2.2	N	N
16	107089	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.66	0.43	37.9	10.5	N	87	1.6	N	N
17	128608	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.96	0.64	45	11	N	96	1.5	N	N
18	119165	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.794	1.2	45.6	11	N	98	2.36	N	N
19	109021	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.8	0.59	43.2	11	N	98	2.1	N	144
20	109814	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.98	1.42	100	11	5-7PC	96	6.3	N	N
21	407643	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.25	0.38	66.55	12	N	98	2.1	N	N
22	8076	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.36	1.56	100.4	11.2	N	102	1.6	4.34/THAL MAJOR	N
23	136012	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.51	0.57	32.9	10.4	PRO3+	102	3.3	N	N
24	109491	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.2	0.44	30.01	12	PRO2+	96	3.6	N	N
25	138044	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	2.42	0.69	32.7	10	PRO3+	86	10.43	N	N
26	72798	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
27	110892	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.35	0.94	36.55	12	BACTERIA	92	1.1	N	x
28	196801	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.38	1.5	45.38	10.2	8-10PC	98	2.1	N	N
29	121260	Y	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	0.27	0.66	84.63	10.8	N	86	1.87	N	N
30	111096	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.25	1.09	40.5	11.2	N	99	1.6	N	N
31	108961	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.58	1.4	130	12.3	BACTERIA	96	1.2	N	N
32	6482	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.65	0.66	46.9	10.9	N	102	1.6	N	N
33	198102	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.25	1.85	37.1	9.6	N	108	10.18	N	N
34	109380	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35	108912	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.85	1.41	62	13	N	86	2.4	N	N
36	66227	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.3	0.78	30	12	N	96	1.5	N	N
37	120475	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.14	1.24	62	10.2	N	102	2	N	N
38	109628	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.64	0.87	51	10.8	5-6PC	98	1.6	N	N
39	103160	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.05	2.05	39.4	11.2	N	97	2.1	N	N
40	901321	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.03	0.77	44	10.2	N	100	1.5	N	N
41	121880	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.58	0.84	43	13.2	N	98	1.6	N	N
42	109864	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	2.72	1.67	138	11.2	N	102	2.1	N	N
43	628867	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.3	0.99	93.15	12.6	N	100	1.9	N	N
44	102234	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
45	102244	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.68	0.88	47.9	8.9	N	92	1.3	N	N
46	109681	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	3.03	0.9	60	10	N	89	1.2	4.2/BETA THAL MINOR	N
47	525644	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.78	1.2	69	11.2	N	92	2.1	N	N

S.NO	MRD NO	NT/NB	CRL (mm)	GESTATIONAL AGE	LEFT UTERINE PI	RIGHT UTERINE PI	UTERINE ARTERY DOPPLER	ANOMALY SCAN	USG FOR FGR (32-34 WKS)	LFT	RFT	SPOT P:C	LDH	URIC ACID
1	134108	0.9/+	51	12W1D	1.67	1.73	1.7	N	FGR-I	N	N	0.6	288	4.5
2	135621	2.1/+	78	13W5D	2.6	1.72	2.16	N	N	N	N	0.4	284	7
3	807729	1.19/+	60.6	12W3D	2	2	2	N	N	-	-	-	-	-
4	112496	1.7/+	60.6	12W2D	1.2	1.12	1.16	N	N	-	-	-	-	-
5	113307	1.3/+	67	13W	1.5	1.8	1.65	N	N	-	-	-	-	-
6	130841	1.7/+	56	12W2D	1	1.4	1.2	N	N	-	-	-	-	-
7	123086	2.2/+	67.2	13W	3.2	3.08	3.14	N	NOT DONE	N	N	6	288	6
8	149962	1.04/+	64	12W2D	1.6	2	1.8	N	N	-	-	-	-	-
9	595120	2.3/+	68.6	13W1D	1.7	1.64	1.67	N	N	-	-	-	-	-
10	184712	1.3/+	55	12W3D	1.1	1.05	1.075	N	N	-	-	-	-	-
11	105336	2.04/+	47.4	11W4D	0.92	1.02	0.97	N	N	-	-	-	-	-
12	959050	1.8/+	49	12W2D	1.4	1.03	1.215	N	N	OT68,PT 90	-	-	-	-
13	106699	0.9/+	46	11W3D	1.7	1.9	1.8	N	N	-	-	-	-	-
14	119162	1.7/+	40.7	11W	0.9	1.2	1.05	N	N	-	-	-	-	-
15	109893	1.2/+	69	12W6D	1.8	1.1	1.45	N	N	-	-	-	-	-
16	107089	1/+	51	12W1D	2.8	1.6	2.2	N	N	-	-	-	-	-
17	128608	1.2/+	48.2	11W4D	1.6	1.9	1.75	N	N	-	-	-	-	-
18	119165	1.9/+	72.3	13W2D	1.4	1.12	1.26	N	N	-	-	-	-	-
19	109021	1.1/+	55	12W3D	1.6	1.8	1.74	N	N	-	-	-	-	-
20	109814	2.1/+	66.5	12W5D	1	0.8	0.9	N	N	-	-	-	-	-
21	407643	1.58/+	52	11W6D	1.8	1.36	1.58	N	N	-	-	-	-	-
22	8076	2.2/+	65	12W6D	1.2	1.1	1.15	N	N	-	-	-	-	-
23	136012	1.6/+	63	12W1D	1.8	1.86	1.83	N	FGR-I	N	N	0.6	285	5.2
24	109491	1.3/+	53.2	13W	1.7	2.1	1.9	N	N	N	N	0.8	270	4.7
25	138044	1.5/+	60.2	12W3D	2.5	1.54	2.02	N	FGR-I	N	N	1.2	298	1.2
26	72798	-	-	-	-	-	-	-	-	-	-	-	-	-
27	110892	1/+	58	12W3D	1.4	0.8	1.1	CLEFT LIP,CLEFT PALATE	X	N	N	0.2	252	3.2
28	196801	1.6/+	39	11W3D	1.4	1	1.2	N	N	-	-	-	-	-
29	121260	1.2/+	63	12W5D	1.91	0.82	0.96	N	N	-	-	-	-	-
30	111096	1.6/+	62	11W4D	1.5	1.3	1.4	N	N	-	-	-	-	-
31	108961	1.7/+	65	12W5D	1.5	2.62	2.06	N	N	-	-	-	-	-
32	6482	2.1/+	55	11W6D	1.2	0.82	1.01	N	X	-	-	-	-	-
33	198102	1.9/+	49.3	11W3D	1.3	0.4	0.65	N	N	-	-	-	-	-
34	109380	-	-	-	-	-	-	-	-	-	-	-	-	-
35	108912	2.0/+	62	12W5D	1.9	2.8	2.35	N	N	-	-	-	-	-
36	66227	2.3/+	66	12W5D	1.6	1.4	1.5	N	FGR-1,OLIGO	-	-	-	-	-
37	120475	2.0/+	62	12W2D	0.9	0.9	0.9	N	N	-	-	-	-	-
38	109628	1.6/+	58	12W2D	0.7	0.6	0.65	N	N	-	-	-	-	-
39	103160	2.2/+	61	11W3D	1.8	1.9	1.85	N	N	-	-	-	-	-
40	901321	1.6/+	63	12W1D	1.5	0.9	1.2	N	N	-	-	-	-	-
41	121880	2.3/+	59	12W6D	1.7	1.9	1.8	N	N	-	-	-	-	-
42	109864	1.46/+	67.7	12W6D	1.2	0.8	2	NOT DONE	NOT DONE	-	-	-	-	-
43	628867	2.1/+	86	13W	1	0.8	0.9	N	N	-	-	-	-	-
44	102234	-	-	-	-	-	-	-	-	-	-	-	-	-
45	102244	2.0/+	63.7	13W1D	1.9	0.96	1.43	N	N	-	-	-	-	-
46	109681	1.7/+	60.2	12W4D	1		1.08	N	OLIGO	-	-	-	-	-
47	525644	1.6/+	64	12W4D	1.5	0.66	1.55	N	N	-	-	-	-	-

S.NO	MRD NO	BIRTH WEIGHT	IF CRIED	SEX	ABNORMALITIES	NICU ADMISSION	INDICATION FOR NICU ADMISSION	MODE OF DELIVERY	INDICATION IF CAESAREAN DONE
1	134108	1.5	Y	F	NO	Y	RESPIRATORY DISTRESS	LSCS	FETAL DISTRESS
2	135621	2.2	Y	F	NO	Y	PREMATURITY	VD	-
3	807729	2.8	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
4	112496	3.2	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
5	113307	3.01	Y	F	NO	NO	-	LSCS	SCAR TENDERNESS
6	130841	3.1	Y	M	NO	NO	-	VD	-
7	123086	1.1	Y	M	NO	Y	PREMATURITY	LSCS	IMPENDING ECLAMPSIA
8	149962	2.6	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
9	595120	3.6	Y	M	NO	NO		LSCS	REFUSAL FOR TOLAC
10	184712	3.3	Y	F	NO	NO	-	VD	-
11	105336	3.2	Y	F	NO	NO	-	LSCS	SCAR TENDERNESS
12	959050	2.8	Y	M	NO	NO	-	VD	-
13	106699	3.1	Y	M	NO	NO	-	LSCS	FETAL DISTRESS
14	119162	2.5	DELAYED	F	NO	Y	DELAYED CRY, CONGENITAL MYOTONIC DYSTROPHY	LSCS	REFUSAL FOR TOLAC
15	109893	2.7	Y	M	NO	NO	-	LSCS	PREVIOUS LSCS WITH BREECH IN LABOUR
16	107089	2.26	Y	F	NO	Y	MECONIUM STAINED LIQUOR	VD	-
17	128608	3	Y	M	NO	NO	-	VD	-
18	119165	3.04	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
19	109021	3.4	Y	M	NO	NO	-	LSCS	FETAL DISTRESS
20	109814	3.2	Y	M	NO	NO		NVD	-
21	407643	3.1	Y	M	NO	NO	-	VD	-
22	8076	2.48	Y	F	NO	NO	-	LSCS	REFUSAL FOR TOLAC
23	136012	1.8	Y	M	NO	Y	PREMATURITY	VD	-
24	109491	2	Y	M	NO	Y	FGR-1	VD	-
25	138044	5.3	Y	M	NO	Y	PREMATURITY	VD	-
26	72798	-	-	-	-	-	-	-	-
27	110892	0.44	NO	M	CLEFT LIP,CLEFT PALATE	NO	-	2ND TRIMESTER EVACUATION	-
28	196801	0.8	NO	M	NO	NO	-	EVACUATION	-
29	121260	3.36	Y	M	NO	NO	-	LSCS	ARREST OF DESCENT IN SECOND STAGE
30	111096	3.2	Y	M	NO	NO	-	VD	-
31	108961	2	Y	F	NO	Y	RESPIRATORY DISTRESS	LSCS	ANHYDRAMNIOS WITH FETAL DISTRESS
32	6482	0.32	NO	F	NO	NO	-	2ND TRIMESTER EVACUATION	-
33	198102	3.3	Y	F	NO	NO	-	VD	-
34	109380	-	-	-	-	-	-	-	-
35	108912	3.2	Y	M	NO	NO	-	LSCS	FETAL DISTRESS
36	66227	3.06	Y	M	NO	FGR-1	-	LSCS	SCAR TENDERNESS
37	120475	3.2	Y	F	NO	NO	-	VD	-
38	109628	2.2	Y	M	NO	FGR-1	-	VD	-
39	103160	2.76	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
40	901321	3.1	Y	F	NO	NO	-	LSCS	SCAR TENDERNESS
41	121880	2.5	Y	M	NO	NO	-	LSCS	FETAL DISTRESS
42	109864	0.66	NO	M	DUPLICATION OF SHORT ARM CHROMOSOME 16	NO	-	VD	-
43	628867	2.58	Y	M	NO	NO	-	VD	-
44	102234	-	-	-	-	-	-	-	-
45	102244	3.42	Y	M	NO	NO	-	LSCS	ARREST OF DESCENT IN SECOND STAGE
46	109681	2.2	Y	F	NO	Y	ANHYDRAMNIOS	LSCS	ANHYDRAMNIOS WITH FETAL DISTRESS
47	525644	3.2	Y	M	NO	NO	-	VD	-

S.NO	MRD NO	GESTATION AT DELIVERY	PREGNANCY OUTCOME	GEATATION OF APPEARANCE OF HTN	GESTATION OF APPEARANCE OF PROTEINURIA	PREECLAMPSIA	EOPE/LOPE	OUTCOME	AMNIOCENTESIS/CVS	FOETAL DNA (cff DNA OR NIPT)
1	134108	35W	PRETERM	34	34	Y	LOPE	PREECLAMPSIA	NO	NO
2	135621	34W1D	PRETERM	30	30	Y	EOPE	PREECLAMPSIA	NO	NO
3	807729	37W5D	TERM	NO	NO	NO	-	NORMAL	NO	NO
4	112496	38W	TERM	NO	NO	NO	-	NORMAL	NO	NO
5	113307	37W4D	TERM	NO	NO	NO	-	NORMAL	NO	NO
6	130841	38W1D	TERM	36	NO	NO	-	NORMAL	NO	NO
7	123086	30W	PRETERM	24	24	Y	EOPE	PREECLAMPSIA	NO	NO
8	149962	37W5D	TERM	NO	NO	NO	-	NORMAL	NORMAL	NO
9	595120	38W	TERM	NO	NO	NO	-	NORMAL	NO	NO
10	184712	38W6D	TERM	NO	NO	NO	-	DOWN SYNDROME	FISH T21	NO
11	105336	39W	TERM	NO	NO	NO	-	NORMAL	NO	NO
12	959050	38W1D	TERM	NO	NO	NO	-	NORMAL	NO	NO
13	106699	39W5D	TERM	NO	NO	NO	-	NORMAL	NO	NO
14	119162	36W1D	PRETERM	NO	NO	NO	-	DOWN SYNDROME	REFUSED	REFUSED
15	109893	35W4D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
16	107089	38W5D	TERM	NO	NO	NO	-	NORMAL	NO	NO
17	128608	38W	TERM	NO	NO	NO	-	NORMAL	NO	NO
18	119165	38W5D	TERM	NO	NO	NO	-	NORMAL	NO	NO
19	109021	39W3D	TERM	NO	NO	NO	-	NORMAL	NO	NO
20	109814	40W	TERM	NO	NO	NO	-	NORMAL	NO	NO
21	407643	39W1D	TERM	NO	NO	NO	-	NORMAL	NORMAL	NO
22	8076	37W	TERM	NO	NO	NO	-	NORMAL	NO	NO
23	136012	34W	PRETERM	30W	30W	Y	LOPE	PREECLAMPSIA	NO	NO
24	109491	36W	PRETERM	35W	35W	Y	LOPE	PREECLAMPSIA	NO	NO
25	138044	32W	PRETERM	28W	28W	Y	EOPE	PREECLAMPSIA	NO	NO
26	72798	-	-	-	-	-	-	-	-	-
27	110892	20W6D	EVACUATION	20W	NO	NO	-	NORMAL	NO	NO
28	196801	17WK	EVACUATION	NO	NO	NO	-	NORMAL	NO	NO
29	121260	39W5D	TERM	NO	NO	NO	-	NORMAL	NO	NO
30	111096	37W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
31	108961	36W2D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
32	6482	20W	EVACUATION	NO	NO	NO	-	NORMAL	NO	NO
33	198102	38W	TERM	NO	NO	NO	-	NORMAL	NO	NORMAL
34	109380	-	-	-	-	-	-	-	-	-
35	108912	37W3D	TERM	NO	NO	NO	-	NORMAL	NO	NO
36	66227	37W5D	TERM	NO	NO	Y	LOPE	PREECLAMPSIA	NO	NO
37	120475	38W4D	TERM	NO	NO	NO	-	NORMAL	NO	NO
38	109628	37W1D	TERM	NO	NO	NO	-	NORMAL	NO	NO
39	103160	37W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
40	901321	37W6D	TERM	NO	NO	NO	-	NORMAL	NO	NO
41	121880	38W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
42	109864	23W3D	PRETERM	NO	NO	NO	-	DUPLICATION OF SHORT ARM CHROMOSOME 16	SIGNIFICANT GENOMIC DUPLICATION OF 7.8 Mb ON SHORT ARM OF CHR 11	NO
43	628867	36W6D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
44	102234	-	-	-	-	-	-	-	-	
45	102244	38W1D	TERM	NO	NO	NO	-	NORMAL		NO
46	109681	34W5D	PRETERM	NO	NO	NO	-	NORMAL	NORMAL	NO
47	525644	36W6D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO

S.NO	MRD NO	NAME	AGE	BMI	LMP	SBP	DBP	MAP	EDD	ETHNICITY	SOCIO ECONOMIC STATUS	EDUCATION	MENSTRUAL HISTORY	OBS HISTORY	NEONATAL DEATH	COMORBIDITIES		PREVIOUS PE	PREVIOUS PRETERM
48	109813	P	29	23.6	10/05/2021	120	80	93	17/02/2022	ASIANTIC	LOWER MIDDLE	POSTGRADUATE	5D/30D	G3P1L1A1	NO	NO	NO	NO	NO
49	730167	JK	35	24.8	13/05/2021	100	60	73	20/02/2022	ASIANTIC	UPPER	GRADUATE	6D/27D	G2P1L1	NO	NO	NO	NO	PRETERM
50	133468	SJ	29	23.3	15/05/2021	130	70	90	19/02/2022	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	4D/28D	PRIMI	NO	NO	-	NO	NO
51	133860	DJ	27	25	20/05/2021	120	80	93	27/02/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/27D	PRIMI	NO	NO	-	NO	NO
52	122568	RH	35	25.5	20/06/2021	120	80	93	27/03/2022	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	3D/25D	PRIMI	NO	NO	-	NO	NO
53	900706	SP	30	25.2	25/03/2021	120	80	93	01/01/2022	ASIANTIC	LOWER	GRADUATE	3D/30D	G2A1	NO	HYPOTHYROID	NO	NO	NO
54	119728	MK	32	27.6	16/04/2021	100	60	73	23/01/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/30D	G7P1L1A5	NO	NO	NO	NO	NO
55	133068	AB	28	26.3	13/04/2021	120	80	93	20/01/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	G3P1L1A1	NO	NO	NO	NO	NO
56	130362	BB	30	22.8	18/04/2021	126	96	106	25/01/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/30D	PRIMI	NO	RA	-	NO	NO
57	109192	KK	29	29.2	16/04/2021	110	70	83	21/01/2022	ASIANTIC	LOWER MIDDLE	GRADUATE	5D/30D	PRIMI	NO	NO	-	NO	NO
58	103039	KK	35	27.3	22/04/2021	120	80	93	27/01/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/30D	G3P1L1A1	NO	NO	NO	NO	NO
59	584960	NA	27	37	16/06/2021	120	80	93	13/03/2022	ASIANTIC	UPPER MIDDLE	POSTGRADUATE	3D/21D	G2P1L0	Y	NO	NO	NO	NO
60	117612	AH	39	24.2	12/06/2021	120	80	93	19/03/2022	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	4D/30D	PRIMI	NO	NO	NO	NO	NO
61	123166	KK	36	24.2	09/08/2021	160	110	127	16/05/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/26D	G3A2	NO	NO	NO	Y	NO
62	128461	GK	28	25	15/10/2021	128	84	97	22/07/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/25D	PRIMI	NO	NO	-	NO	NO
63	121896	JK	32	24.8	10/8/2021	114	78	90	17/05/2022	ASIANTIC	UPPER MIDDLE	POSTGRADUATE	3D/26D	G4A3	NO	NO	NO	NO	NO
64	101733	RK	33	25	02/10/2021	118	72	87	09/07/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/28D	G2P1L1	NO	NO	NO	NO	NO
65	1384192	KS	26	22	10/10/2021	160	110	127	17/07/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/36D	G2P1L1	NO	NO	NO	NO	PRETERM
66	138462	G	28	25	04/11/2021	120	84	96	11/08/2022	ASIANTIC	LOWER	GRADUATE	4D/36D	G2A1	NO	NO	NO	NO	NO
67	120458	S	27	27.2	28/11/2021	190	100	130	04/09/2022	ASIANTIC	UPPER MIDDLE	POSTGRADUATE	5D/30D	PRIMI	NO	NO	NO	NO	NO
68	148961	JK	31	28	17/11/2021	110	70	83	24/08/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/26D	G2P1L1	NO	NO	NO	NO	NO
69	120057	RK	35	25.5	02/10/2021	160	100	120	09/07/2022	ASIANTIC	LOWER MIDDLE	HIGHER SECONDARY	5D/30D	PRIMI	NO	NO	NO	NO	NO
70	157906	PK	36	26.6	04/12/2021	120	80	93	11/09/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/28D	G3P1L1A1	NO	NO	NO	NO	NO
71	102631	S	28	25	28/09/2021	140	90	107	05/07/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/28D	PRIMI	NO	NO	NO	NO	NO
72	102335	SG	27	26.6	04/12/2021	140	80	100	11/09/2022	ASIANTIC	UPPER MIDDLE	POSTGRADUATE	2D/30D	G3P1L1A1	NO	ICP	NO	NO	PRETERM
73	136534	PG	26	24.2	06/12/2021	140	100	113	13/09/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	2D/25D	G3P1L1A1	NO	NO	NO	NO	PRETERM
74	1379381	KK	28	25	09/01/2022	110	70	83	16/10/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/28D	G2A1	NO	NO	NO	NO	NO
75	120578	VK	23	29	29/12/2021	129	86	100	05/10/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/26D	PRIMI	NO	NO	-	NO	NO
76	126105	RB	34	29	27/11/2021	120	80	93	04/09/2022	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	5D/30D	G2P1L1	NO	NO	NO	NO	NO
77	140189	KJ	35	23	05/01/2022	110	70	83	12/10/2022	ASIANTIC	LOWER MIDDLE	GRADUATE	4D/28D	G3P1L1A1	NO	NO	NO	NO	NO
78	104897	PK	30	24	15/01/2022	120	86	97	22/10/2022	ASIANTIC	LOWER	GRADUATE	2D/30D	G2P1L1	NO	NO	NO	NO	NO
79	112304	AK	34	25	16/01/2022	110	70	83	23/10/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/28D	PRIMI	NO	NO	-	NO	NO
80	7930	MJ	32	24.9	27/01/2022	120	80	93	03/11/2022	ASIANTIC	LOWER MIDDLE	HIGHER SECONDARY	3D/28D	G2P1L1	NO	NO	NO	NO	NO
81	132278	NG	33	23.6	20/01/2022	110	70	83	27/10/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	4D/28D	G2P1L1	NO	GDMA1	NO	NO	NO
82	704020	LS	29	24.4	02/02/2022	126	84	98	09/11/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/36D	G2P1L1	NO	NO	NO	NO	NO
83	144911	RK	40	28.7	03/02/2022	120	76	91	10/11/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	3D/28D	G3P1L1A1	NO	NO	NO	NO	NO
84	140691	TS	23	26.6	11/02/2022	110	70	83	18/11/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/31D	G2A1	NO	NO	NO	NO	NO
85	588606	SJ	31	28	14/02/2022	-	-	-	21/11/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/32D	G2P1L1	NO	-	-	NO	NO
86	121506	GJ	33	26	18/02/2021	180	110	133	25/11/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	2D/34D	PRIMI	NO	NO	-	NO	NO
87	95165	SB	30	28	27/02/2022	110	76	87	06/12/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/30D	G3P1L1A1	NO	NO	NO	NO	NO
88	145210	HK	24	24	18/02/2022	120	70	87	25/11/2022	ASIANTIC	LOWER MIDDLE	GRADUATE	3D/25D	PRIMI	NO	NO	-	NO	NO
89	140681	GS	32	24	25/03/2022	160	110	127	30/12/2022	ASIANTIC	UPPER MIDDLE	HIGHER SECONDARY	3D/35D	PRIMI	NO	NO	-	NO	NO
90	120569	SK	30	25.5	17/04/2021	120	70	87	22/01/2022	ASIANTIC	UPPER MIDDLE	GRADUATE	5D/36D	PRIMI	NO	NO	-	NO	NO

S.NO	MRD NO	ABORTIONS	TUBERCULOSIS	MULTIPLE PREGNANCIES	DIABETES	CHROMOSOMAL ABORMALITIES	CONSANGUINOUS MARRIAGE	PREMATURITY	FIRST TRIMESTER SCREENING	FAMILY HISTORY GENETIC DISORDER	FREE BETA-hCG (MoM)	PAPP-A (MoM)	PIGF (pg/ml)	HB	URINE ROUTINE	RBS	TSH	HbA2/HPLC	OGTT
48	109813	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.13	0.78	72	11.2	N	86	2.2	N	N
49	730167	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	0.42	0.3	54	11.9	N	94	2.6	N	N
50	133468	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.88	1.1	70	12	N	84	2.3	N	N
51	133860	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.99	1.2	60	11	N	96	2.1	N	N
52	122568	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	0.95	1.27	72	10.2	N	94	1.3	N	N
53	900706	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.6	0.88	82	9	N	84	4.43	N	N
54	119728	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.89	0.66	43	10.8	N	94	2.3	N	N
55	133068	Y	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.2	0.3	71.74	12	N	86	1.7	N	N
56	130362	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.6	0.88	60	11	N	92	2.01	N	N
57	109192	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.2	0.78	65	11	N	96	1.6	N	N
58	103039	Y	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	2.1	1.97	108	12	N	94	2.08	N	N
59	584960	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.8	1.2	97	9.3	N	98	2.99	N	N
60	117612	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.7	0.99	60	10.7	N	99	2.3	N	N
61	123166	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.2	0.98	22	10	PRO 3+	96	2.1	N	N
62	128461	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.99	1.2	41.75	12	N	99	1.8	N	N
63	121896	Y	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.2	0.3	40	9.8	N	97	1.9	N	N
64	101733	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.87	0.69	35.02	13	8-9PC	104	2.4	N	N
65	1384192	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.57	0.66	28	9.8	PRO 3+	98	2.2	N	N
66	138462	Y	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.3	0.22	54	10.9	N	94	1.9	N	N
67	120458	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.69	1.95	25	11	PRO3+	100	1.7	N	N
68	148961	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.57	1	73	10.2	N	106	2.1	N	N
69	120057	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.434	1.159	15.7	12	PR0 2+	95	1.4	N	N
70	157906	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.74	0.86	53	10.2	N	98	2.1	N	N
71	102631	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.244	0.55	20.5	10	N	85	1.8	N	N
72	102335	Y	Y	NO	NO	NO	NO	NO	HIGH RISK	NO	2.38	0.18	41	11.2	N	86	1.68	N	N
73	136534	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.33	0.89	15	10.8	N	98	1.9	N	N
74	1379381	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.01	0.8	37	10.2	N	96	2.1	N	N
75	120578	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.21	0.83	60.9	11	N	95	1.9	N	N
76	126105	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.2	0.3	48	10	N	87	2.3	N	N
77	140189	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.42	87	92	9.7	N	96	1.4	N	N
78	104897	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.89	1.38	74	10	N	100	1.5	N	N
79	112304	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.2	0.3	98	11	N	97	1.2	N	N
80	7930	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.48	0.82	38	10	N	85	2.1	N	N
81	132278	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.55	1.2	35	12	N	92	2.3	N	143
82	704020	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.2	1.08	29.9	10.2	N	94	2.08	N	N
83	144911	Y	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	1.2	0.25	33	12	N	96	2	N	N
84	140691	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.58	1.06	48	12	N	99	1.2	N	N
85	588606	NO	-	NO	NO	-	NO	-	-	-	-	-	-	-	-	-	-	-	-
86	121506	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.87	1.7	27	11	PRO 3+	88	2.4	N	N
87	95165	Y	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.83	2.54	49	11.3	N	100	2.8	N	N
88	145210	NO	NO	NO	NO	NO	NO	NO	HIGH RISK	NO	2.19	0.71	77	10.9	N	102	4	N	N
89	140681	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	0.89	1.2	22	12.2	PRO 2 +	60	1.5	N	N
90	120569	NO	NO	NO	NO	NO	NO	NO	LOW RISK	NO	1.2	0.3	58	11	N	87	1.6	N	N

S.NO	MRD NO	NT/NB	CRL (mm)	GESTATIONAL AGE	LEFT UTERINE PI	RIGHT UTERINE PI	UTERINE ARTERY DOPPLER	ANOMALY SCAN	USG FOR FGR (32-34 WKS)	LFT	RFT	SPOT P:C	LDH	URIC ACID
48	109813	2.1/+	73	13W2D	1.9	1.36	1.63	N	N	-	-	-	-	-
49	730167	1.5/ABSENT NASAL BONE	51.9	12W1D	1.1	1.6	1.3	ABSENT FUNDIC BUBBLE WITH CORPUS CALLOSUM AGENESIS WITH CHOROID PLEXUS CYST	NOT DONE	-	-	-	-	-
50	133468	2.1/+	57	12W4D	1.2	0.88	1.04	N	N	-	-	-	-	-
51	133860	1.9/+	53	12W	0.9	0.9	0.9	N	N	-	-	-	-	-
52	122568	1.16/+	63	12W4D	2	2.18	2.09	N	N	-	-	-	-	-
53	900706	1.6/+	70	12W	1	1.4	1.2	N	LOOP OF CORD AROUND NECK	-	-	-	-	-
54	119728	1.7/+	62	12W4D	1.62	0.62	0.81	N	OLIGOHYDRAMNIOS	-	-	-	-	-
55	133068	1.8/ABSENT NASAL BONE	61.6	12W3D	0.8	1.8	1.3	N	N	-	-	-	-	-
56	130362	1.9/+	56	12W6D	1.2	2	1.6	N	N	-	-	-	-	-
57	109192	2.1/+	69	12W2D	1	1.4	1.2	N	N	-	-	-	-	-
58	103039	0.98/+	63.8	12W3D	1.6	1.14	1.37	NOT DONE	NOT DONE	-	-	-	-	-
59	584960	1.8/+	66	11W5D	1.8	0.8	1.35	N	N	-	-	-	-	-
60	117612	2.1/+	63.4	12W5D	1.3	1.82	1.56	RIGHT CHOROID PLEXUS CYST 4X4MM	N	-	-	-	-	-
61	123166	1.9/+	68	13W1D	2.4	2.6	2.5	N	OLIGOHYDRAMNIOS, UTEROPLACENTAL INSUFFICIENCY	N	N	0.6	255	5
62	128461	1.8/+	66.7	13W	1.1	0.92	1.01	N	N	-	-	-	-	-
63	121896	2.1/+	78.4	13W6D	1.48	0.48	0.74	N	N	-	-	-	-	-
64	101733	1.7/+	66	13W	0.9	0.54	1.2	N	N	-	-	-	-	-
65	1384192	1.9/+	69	13W1D	1.2	2.6	1.9	N	FGR I, UTEROPLACENTAL INSUFFICIENCY	N	N	10	285	5.2
66	138462	2.4/+	67.4	13W1D	0.8	0.56	0.68	N	N	-	-	-	-	-
67	120458	2.4/+	51.7	11W6D	1.5	2.42	1.96	N	REVERSAL OF UMBILICAL ARTERY FLOW	N	N	9.2	300	5.8
68	148961	2.1/+	78	12W6D	2	1.4	1.7	N	N	-	-	-	-	-
69	120057	1.2/+	59	12W3D	2.1	2.1	2.08	N	FGR I	-	-	-	-	-
70	157906	1.3/+	55	12W4D	0.9	1.2	1.05	N	N	-	-	-	-	-
71	102631	1.3/+	63.5	12W5D	1.6	1.48	1.54	N	N	-	-	-	-	-
72	102335	1.1/+	68.1	13W3D	1.8	1.6	1.7	N	N	OT 65,PT 79	-	-	-	-
73	136534	1.8/+	58	12W3D	1.8	2	1.9	N	N	-	-	-	-	-
74	1379381	1.3/+	51	11W6D	0.9	1.5	1.2	N	N	-	-	-	-	-
75	120578	1.6/+	54	12W	1.8	0.8	1.3	N	N	-	-	-	-	-
76	126105	2.1/+	67	12W	1.1	0.7	0.9	N	N	-	-	-	-	-
77	140189	1.8/+	62.4	12W4D	1.5	1.72	1.61	N	N	-	-	-	-	-
78	104897	1.3/+	69	13W2D	1.6	1.6	1.6	N	N	-	-	-	-	-
79	112304	2.8/ABSENT NASAL BONE	76.5	13W5D	1.6	0.8	1.2	N	N	-	-	-	-	-
80	7930	1.6/+	57	12W3D	2	2.5	2.25	N	N	-	-	-	-	-
81	132278	2.0/+	75	13W4D	1	1.2	1.1	N	N	-	-	-	-	-
82	704020	2.1/+	55	11W5D	1.6	1.1	1.35	N	N	-	-	-	-	-
83	144911	1.5/+	54.5	12W2D	1.6	0.8	1.2	N	NOT DONE	-	-	-	-	-
84	140691	1.9/+	62	12W3D	1	1.4	1.2	N	N	-	-	-	-	-
85	588606	-	-	-	-	-	-	-	-	-	-	-	-	-
86	121506	1.9/+	46	12W	3	2.6	2.8	N	N	N	N	3	296	4.8
87	95165	1.7/+	60.9	12W3D	1.9	1	1.45	N	N	-	-	-	-	-
88	145210	2.1/+	69	13W3D	1.6	1.4	1.5	N	N	-	-	-	-	-
89	140681	1.6/+	58	12W2D	2	2.4	2.2	N	FGR II	N	N	5.87	200	5.1
90	120569	1.5/+	76.5	13W5D	1.9	2.3	2.1	NOT DONE	NOT DONE	-	-	-	-	-

S.NO	MRD NO	BIRTH WEIGHT	IF CRIED	SEX	ABNORMALITIES	NICU ADMISSION	INDICATION FOR NICU ADMISSION	MODE OF DELIVERY	INDICATION IF CAESAREAN DONE
48	109813	3.2	Y	M	NO	NO	-	VD	-
49	730167	0.4	NO	M	EDWARD SYNDROME	NO	-	EVACUATION	-
50	133468	3.3	Y	M	NO	NO	-	VD	-
51	133860	3.2	Y	M	NO	NO	-	VD	-
52	122568	3.2	Y	M	NO	NO	-	LSCS	FETAL DISTRESS
53	900706	2.78	Y	M	NO	NO	-	LSCS	FAILED INDUCTION
54	119728	2.09	Y	M	NO	NO	-	LSCS	MATERNAL CONDITION
55	133068	3	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
56	130362	2.9	Y	M	NO	NO	-	VD	-
57	109192	3.94	Y	M	NO	Y	MECONIUM ASPIRATION	LSCS	MSL WITH FETAL DISTRESS
58	103039	0.12	NO	M	IUD	NO	-	EVACUATION	-
59	584960	4.36	Y	M	NO	NO	-	VD	-
60	117612	3.3	Y	F	NO	NO	-	VD	-
61	123166	1.1	Y	F	NO	Y	FGR,PREMATURITY	LSCS	FETAL DISTRESS
62	128461	3.2	Y	F	NO	NO	-	VD	-
63	121896	2.9	Y	M	NO	NO	-	LSCS	APH WITH FETAL DISTRESS
64	101733	3.5	Y	F	NO	NO	-	LSCS	FAILURE OF INDUCTION
65	1384192	1	Y	M	NO	Y	PREMATURITY, FGR	LSCS	IMPENDING ECLAMPSIA WITH ABNORMAL DOPPLER
66	138462	1.72	Y	F	NO	Y	PREMATURITY	LSCS	FETAL DISTRESS
67	120458	0.7	Y	M	NO	Y	PREMATURITY/ABNORMAL DOPLLER	LSCS	REVERSAL OF UMBILICAL ARTERY FLOW
68	148961	3.8	Y	M	NO	NO	-	LSCS	MSL WITH FETAL DISTRESS
69	120057	1	Y	F	NO	Y	PREMATURITY/FGR	LSCS	NON REASSURING NST
70	157906	3.26	Y	M	NO	NO	-	VD	-
71	102631	2.9	Y	F	NO	NO	-	VD	-
72	102335	3.3	Y	M	NO	NO	-	LSCS	FETAL DISTRESS
73	136534	2.6	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
74	1379381	3.34	Y	M	NO	NO	-	LSCS	SCAR TENDERNESS
75	120578	3.1	Y	F	NO	NO	-	VD	-
76	126105	3.16	Y	M	NO	NO	-	VD	-
77	140189	3.2	Y	F	NO	NO	-	VD	-
78	104897	3.4	Y	M	NO	NO	-	LSCS	APH WITH FETAL DISTRESS
79	112304	0.06	NO	M	NO	NO	-	MTP	-
80	7930	2.8	Y	F	NO	NO	-	LSCS	SCAR TENDERNESS
81	132278	3.1	Y	F	NO	NO	-	LSCS	FETAL DISTRESS
82	704020	3.062	Y	F	NO	NO	-	LSCS	REFUSAL FOR TOLAC
83	144911	0.2	NO	M	NO	NO	-	MTP	-
84	140691	2.76	Y	M	NO	NO	-	VD	-
85	588606	-	-	-	-	-	-	-	-
86	121506	1	Y	F	NO	Y	PREMATURITY	LSCS	IMPENDING ECLAMPSIA
87	95165	3.8	Y	F	NO	NO	-	LSCS	SCAR TENDERNESS
88	145210	3.1	Y	M	NO	NO	-	VD	-
89	140681	0.9	Y	M	NO	Y	ABNORMAL DOPPLER/PREMATURITY	LSCS	IMPENDING ECLAMPSIA WITH ABSENT FLOW
90	120569	0.06	NO	F	NO	NO	-	EVACUATION	-

S.NO	MRD NO	GESTATION AT DELIVERY	PREGNANCY OUTCOME	GEATATION OF APPEARANCE OF HTN	GESTATION OF APPEARANCE OF PROTEINURIA	PREECLAMPSIA	EOPE/LOPE	OUTCOME	AMNIOCENTESIS/CVS	FOETAL DNA (cff DNA OR NIPT)
48	109813	37W4D	TERM	NO	NO	NO	-	NORMAL	NO	NO
49	730167	19W4D	EVACUATION	NO	NO	NO	-	TRISOMY 18	TRISOMY 18	NO
50	133468	39W	TERM	NO	NO	NO	-	NORMAL	NO	NO
51	133860	39W	TERM	NO	NO	NO	-	NORMAL	NO	NO
52	122568	38W4D	TERM	NO	NO	NO	-	NORMAL	NO	NORMAL
53	900706	37W	TERM	NO	NO	NO	-	NORMAL	NO	NO
54	119728	37W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
55	133068	38W	TERM	NO	NO	NO	-	NORMAL	NO	NORMAL
56	130362	37W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
57	109192	39W4D	TERM	NO	NO	NO	-	NORMAL	NO	NO
58	103039	17W	EVACUATION	NO	NO	NO	-	EDWARD SYNDROME	EDWARD SYNDROME	NO
59	584960	39W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
60	117612	39W3D	TERM	NO	NO	NO	-	NORMAL	NO	NO
61	123166	30W6D	PRETERM	21W2D	21W	Y	EOPE	PREECLAMPSIA	NO	NO
62	128461	39W	TERM	NO	NO	NO	-	NORMAL	NO	NO
63	121896	36W4D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
64	101733	39W3D	TERM	NO	NO	NO	-	NORMAL	NO	NO
65	1384192	32W2D	PRETERM	28W	28W	NO	-	NORMAL	NO	NO
66	138462	33W	PRETERM	NO	NO	NO	-	NORMAL	NO	NORMAL
67	120458	28W	PRETERM	26W	26W	Y	EOPE	PREECLAMPSIA	NO	NO
68	148961	40W	TERM	NO	NO	NO	-	NORMAL	NO	NO
69	120057	34W2D	PRETERM	22W	22W	Y	EOPE	PREECLAMPSIA	NO	NO
70	157906	38W1D	TERM	NO	NO	NO	-	NORMAL	NO	NO
71	102631	36W1D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
72	102335	37W6D	TERM	NO	NO	NO	-	NORMAL	NORMAL	NO
73	136534	39W4D	TERM	NO	NO	NO	-	NORMAL	NO	NO
74	1379381	38W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
75	120578	38W1D	TERM	NO	NO	NO	-	NORMAL	NO	NO
76	126105	40W1D	TERM	NO	NO	NO	-	NORMAL	NO	NORMAL
77	140189	39W	TERM	NO	NO	NO	-	NORMAL	NO	NO
78	104897	38W2D	TERM	NO	NO	NO	-	NORMAL	NO	NO
79	112304	14W6D	EVACUATION	NO	NO	NO	-	DOWN SYNDROME	FISH T21	NO
80	7930	36W5D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
81	132278	37W3D	TERM	NO	NO	NO	-	NORMAL	NO	NO
82	704020	40W	TERM	NO	NO	NO	-	NORMAL	NO	NO
83	144911	19W	IUD	NO	NO	NO	-	DOWN SYNDROME	FISH T21	NO
84	140691	38W6D	TERM	NO	NO	NO	-	NORMAL	NO	NO
85	588606	-	-	-	-	-	-	-	-	-
86	121506	30W1D	PRETERM	NO	NO	NO	-	NORMAL	NO	NO
87	95165	37W3D	TERM	NO	NO	NO	-	NORMAL	NO	NO
88	145210	38W3D	TERM	NO	NO	NO	-	NORMAL	NORMAL	NO
89	140681	27W6D	PRETERM	25W	25W	Y	EOPE	PREECLAMPSIA	NO	NO
90	120569	13W6D	EVACUATION	NO	NO	NO	-	NORMAL	NO	NO

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No. BFUHS/2K21p-TH/ 145 Date 05/01/22

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Mehak Arora**, a student of your college for **MD Obstetrics & Gynaecology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Predictive value of first trimester screening combined with plgf and uterine artery pulsatility index for preeclampsia and aneuploidy.

Supervisor

Dr. Ashima Taneja
Prof. & Head,
Dept. of Obst. & Gynae.,
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Co-Supervisor

Dr. Navjot Kaur Bajwa
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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

75. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
76. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

OBSTETRICS & GYNAECOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH, 2021

DR. MEHAK ARORA

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY
For the degree of	MD (Obstetrics & Gynaecology)
Name of the candidate	Dr. Mehak Arora
Supervisor	Dr. Ashima Taneja, Professor & Head, Department of Obstetrics & Gynaecology, DMCH, Ludhiana
Co-supervisor(s)	Dr. Navjot Kaur Bajwa, Professor & Head, Biochemistry, DMC&H, Ludhiana Dr. Kanupriya Jain, Associate Professor, Obsetrics & Gynaecology, DMC&H, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: First trimester screening is a non invasive method of prenatal testing done at 10-14 weeks for detection of aneuploidy. Preeclampsia which occurs in 2-8% of all pregnancies is a significant cause of maternal morbidity and mortality and fetal complications. First trimester screening which includes - PAPP-A, free Beta-hCG, with ultrasound for Nuchal Translucency can be combined with PIGF and Uterine artery doppler which help in early prediction of aneuploidy and preeclampsia respectively.

Aim of Study: To study the predictive value of first trimester screening combined with PIGF and Uterine artery Doppler for preeclampsia and aneuploidy.

Materials & methods: Pregnant women at or between 11-14 weeks period of gestation attending the outpatient clinic or admitted will be randomly selected,screened and followed up till delivery. The ones subjected to first trimester screening and PIGF testing with uterine artery doppler will be analysed for aneuploidy and preeclampsia.

Clinical Significance: First trimester screening which includes beta hCG and PAPP-A and an ultrasound for nuchal translucency has a detection rate of 90% for aneuploidy. PIGF combined with ultrasound for uterine artery doppler has been recently introduced to detect preeclampsia in first trimester. Preeclampsia is a significant cause of maternal morbidity and mortality and fetal complications. High uterine artery pulsatility index is a predictor of pre-eclampsia.

Keywords: First trimester screening, aneuploidy, preeclampsia

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY"** exist in the Department of Obstetrics and Gynaecology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

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Place : LUDHIANA

Date : 18/03/2021

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Mehak Arora
Department	Obstetrics & Gynaecology
Topic of Thesis	PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY
Likely date of appearing in PG examination	June 2023
Date of enrollment	30th June, 2020
Name of Head of Department	Dr. Ashima Taneja
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Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
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	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairman
Ethics Committee

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PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Mehak Arora 142-L Model Town, Ludhiana, Punjab 141002
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD OBSTETRICS AND GYNAECOLOGY
4	DATE OF ADMISSION OF COURSE	25TH JULY 2020
5	TITLE OF THE TOPIC	PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PlGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Aneuploidy is presence of abnormal number of chromosomes in a cell and occurs in 1 in 160 live births. Most common aneuploidies are trisomies which form 0.3% of live births. Most common trisomy involves chromosome 21 or Down's syndrome. It causes intellectual disability, cardiac disorders, gastrointestinal and other organ dysfunctions. Other trisomies include 18, 13 also known as Edward's and Patau's syndrome respectively. Prenatal screening is done in first trimester to detect aneuploidy and risk of preeclampsia. First trimester screening is a non-invasive method of prenatal genetic testing done at 11 to 13^{+6}weeks of gestation, for the early detection of aneuploidy in pregnancies.

This study combines first trimester screening which includes serum biomarkers produced by maternal placenta, yolk sac and fetal liver tissue i.e.

PAPP-A (Pregnancy Associated Plasma Protein)

Free Beta-hCG(Beta-human chorionic gonadotropin) and

An ultrasound for Nuchal Translucency (NT) combined with PlGF(Placental Growth Factor) and Uterine artery pulsatility index(Ut PI) using uterine artery doppler. High pulsatility index of uterine artery is a predictor of pre-eclampsia that can occur later in pregnancy.

Preeclampsia occurs in 2-8% of all pregnancies and is a significant cause of maternal morbidity and mortality especially in developing countries. It also increases the risk of fetal complications such as Fetal Growth Restriction (FGR), low birth weight, preterm birth and perinatal death.

PAPP-A and PLGF are useful in screening for aneuploidies in combination with maternal age, fetal NT, maternal serum free beta hCG at 11-13 weeks' gestation. If these serum markers prove to have a predictive value for Downs syndrome as well as preeclampsia then these could be screened by combination strategy at the same time in first trimester.

This study is conducted to evaluate the predictive value of first trimester screening combined with Placental growth factor(PlGF) and Uterine artery pulsatility index (Ut PI) using uterine artery doppler for detection of preeclampsia and aneuploidy. It is suggested that high detection rate in first trimester can provide accurate information regarding short and long term prognosis, recurrence risk, counselling and optimising the outcome.

USG done at 11-13^{+6} weeks for nuchal translucency and uterine artery PI will help in prediction of aneuploidy and pre eclampsia respectively.

This study is an attempt to show reduction in time to diagnosis of pre eclampsia. More timely management particularly relating to targeted surveillance of women at increased risk, could help in reduction of maternal adverse events.

Moreover, this type of screening for aneuploidies will ensure informed decision making, timely access to a screening test and allows patients follow up testing and access to an intervention.

6.2 REVIEW OF LITERATURE

Prenatal screening for trisomies based on the analysis of biochemical markers in maternal serum has become an established part of obstetric practice in many countries. The prenatal screening for trisomies focuses on the first trimester more than second trimester because it provides clinicians and patients with substantial advantage of an earlier diagnosis.[1] It can be combined with ultrasound at 11-14 weeks for nuchal translucency and Uterine Artery Pulsatility index. This will help in early prediction of aneuploidy and preeclampsia respectively.

SERUM BIOMARKERS

A number of proteins in the maternal circulation have been found during the time of pregnancy,many of which are modified by placenta. Differences in levels of some proteins have been observed in patients developing pre eclampsia and the ones carrying a foetus with a chromosomal abnormality.[2,3]

The levels of these proteins change during pregnancy so interpretation requires knowledge of gestational ages. For example, differences in protein levels may be observed during second trimester but not the first, while other proteins show differences during first trimester but not the second.

MATERNAL SERUM PAPP-A: PAPP-A is one of the two maternal serum markers currently used for screening between 10 and 14 weeks.[2] It is produced by the placental syncytiotrophblast and deciduas. It increases the bioavailability of insulin like growth factor, which in turn mediate trophoblast invasion and modulates glucose and amino acids transport in the placenta.

PAPP-A is also expressed in ovarian granulosa cells and in non reproductive tissues such as fibroblasts,osteoblasts etc.[4,5] Low first trimester PAPP-A levels are associated with trisomies and non-Down syndrome aneuploidies and also with increased risk of pre eclampsia.[6,7]

Methods: ECLIA (Electro chemiluminescence Immunoassay) by Roche e411

MATERNAL SERUM FREE BETA-hCG HORMONE

Human chorionic gonadotropin is 39,500-Da glycoprotein hormone normally found in blood and urine only during pregnancy. For the initiation and maintenance of pregnancy, beta-hCG mediates multiple placental, uterine and fetal functions. The free beta-hCG circulating in maternal serum corresponds to only 0.3-4% of total hCG. Abnormal secretory function in severe pre eclampsia is associated with elevated serum beta-hCG levels. First trimester serum beta-hCG levels are increased in Down syndrome as well as trisomy 18 and 13.[2,8,9]

Methods: ECLIA(Electro chemiluminescence Immunoassay) by Roche e411

MATERNAL SERUM PLACENTAL GROWTH FACTOR (PlGF):

Placental growth factor is a glycosylated dimeric glycoprotein, which is a member of the vascular endothelial growth factor (VEGF) sub-family. PlGF is synthesised in villous and extravillous cytotrophoblast and has both vasculogenetic and angiogenetic functions. It is believed to contribute a change in angiogenesis from a branching to a non-branching phenotype controlling the expansion of the capillary network. Its angiogenetic abilities have been speculated to play a role in normal pregnancy, and changes in the levels of PlGF or its inhibitory receptor have been implicated in the development of PE.

Preeclampsia is associated with reduced placental production of PlGF, and several studies reported that during the clinical phase of PE, the maternal serum PlGF concentration is reduced.[3,10] These reduced levels of serum PlGF precede the clinical onset of the disease and are evident in both the first and second-trimesters of pregnancy.[4,6]

Methods: ECLIA(Electro chemiluminescence Immunoassay) by Roche e411

NUCHAL TRANSLUCENCY

One of the markers in first trimester screening for chromosomal abnormalities is measurement of NT thickness between 10 and 14 weeks of gestation.[11-13] NT measures the subcutaneous fluid filled space between the back of spine and skin of fetal neck.

Using NT measurement and maternal age alone 81% of affected pregnancies can be identified with a 5% false positive rate.

The vast majority of fetuses with Down syndrome have an increase in NT measurement when compared to normal fetuses of same gestational age. Increased NT may be associated with miscarriages and abnormal karyotypes.[7,13]

UTERINE ARTERY DOPPLER

Doppler assessment of uterine artery impedance can be performed between 11^{+0} weeks and 13^{+6} weeks' gestation via a transabdominal or transvaginal approach.[14] It can be used to predict risk of preeclampsia in first trimester. Ultrasonographic evidence of Preeclampsia includes an increase in pulsatility index[PI] of uterine artery.[15,16] Increased resistance, typically assessed by pulsatility index may reflect suboptimal placentation. Each uterine artery is identified lateral to the uterus using color doppler at the level of internal os. The Pulsatility index of both uterine ateries is detected and the mean PI is calculated. The mean uterine pulsatility index of both the arteries at 11-13 weeks gestation shows highly significant difference between pre eclamptic women and healthy women.[17] The cut offs for mean Ut PI on transabdominal ultrasound are 1.95,1.79 and 1.62 at 11,12 and 13 weeks respectively.[18] On transvaginal ultrasound the cut offs are 1.88,1.67 and 1.47 at 11,12 and 13 weeks respectively.[18] It has been suggested that patients with high pulsatility index will be administered low dose aspirin at 16 weeks and will be followed for development of preeclampsia and its complications thus making early prediction of preeclampsia important.

The predictive utility of Doppler ultrasound in interrogation of a range of vascular beds has been evaluated but the most commonly used is uterine artery which can be conviniently assessed at the time of 12 week fetal scan.[19]

In a National Institute for Health Research (United Kingdom)–commissioned prospective validation study of the algorithm in 16,747 pregnancies, including 473 (2.8%) women who developed preeclampsia, the screen-positive rate by the NICE method was 10.3%

and the detection rate for all preeclampsia was 30%; for preterm preeclampsia, it was 41%. The detection rate of the mini–combined test (maternal factors, MAP, and PAPP-A) for all preeclampsia was 43%, which was superior to that of the NICE method by 12.1% (95% CI, 7.9–16.2). In screening for preterm preeclampsia by a combination of maternal factors, MAP, UtA-PI, and serum PLGF (FMF triple test), the detection rate was 82%, which was higher than that of the NICE method by 41.6% (95% CI, 33.2–49.9).[20]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To study the predictive value of first trimester screening combined with PlGF and Uterine artery Doppler for preeclampsia and aneuploidy.

7. MATERIAL AND METHODS

7.1 SOURCE OF DATA

A hospital based, prospective clinical study will be conducted on randomly selected patients between 11-14 weeks period of gestation in the department of obstetrics and gynaecology at Dayanand Medical College and Hospital, Ludhiana (Punjab), a tertiary care hospital for a time period of 1 year, from March 2021 to March 2022.

Inclusion criteria

- All pregnant patients in first trimester between 11-14 weeks of gestation.
- Patients consenting to participate in study.
- Singleton pregnancies.
- Non smokers

Exclusion criteria

- Multiple Pregnancies
- Molar pregnancies
- Smokers
- Chronic hypertensive
- Patients on aspirin for any indication

7.2 METHOD OF COLLECTION OF DATA

Pregnant women at or between 11-14 weeks period of gestation attending the outpatient clinic or admitted will be randomly selected, screened and followed up till delivery. An informed and written consent will be taken from all patients before participating in the study with full freedom to leave the study at any time.

A structured predesigned proforma will be used for the study. Detailed history including basic demographics such as age, weight, height, BP etc will be taken. Relevant antenatal history and routine investigations will be recorded as per proforma. Relevant past history and family history will be taken.

Pregnant women at or between 11-14 weeks gestation will be subjected to First Trimester Screening (FTS) which includes

biochemical tests i.e. PAPP- A, free Beta-hCG, USG for NT combined with PlGF and Uterine artery doppler for mean pulsatility index(UtPI). Results will be analysed.

DURATION OF STUDY

This study will be conducted over a period of one year, from March 2021 to March 2022.

OUTCOME

As per the results at the completion of study.

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows

7.3 DOES THE STUDY REQUIRE ANY INTERVENTION TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO PLEASE DESCRIBE BRIEFLY.

LABARATORY INVESTIGATION

FREE BETA-hCG

PAPP-A

PlGF

ROUTINE INVESTIGATIONS

Hb

Urine routine

RBS

TSH

HbA2/HPLC

OGTT

USG :

NT/NB

CRL

GESTATIONAL AGE

UTERINE ARTERY DOPPLER

ANOMALY SCAN

USG FOR FGR (32-34 WKS)

Following tests will be done if needed:

LFT

RFT

SPOT P:C

LDH

URIC ACID

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3

Yes, attached along with..

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PROFORMA

Sr. No

- Name:- Age:- DOB
- Husband's name:- Age:- DOB
- Date of admission:-
- Admission number:-
- MRD number:-
- Residential address:-
- Education:-
- Occupation:-
- Weight:- POG:-
- Height:- BP:-
- LMP:- EDD:-
- **MENSTRUAL HISTORY:-**
- **OBS. HISTORY:-**
- **MULTIPLE PREGNANCY:**
- **DIABETES:-**
- **HYPERTENSION**

PAST HISTORY:

- DIABETES MELLITUS
- TUBERCULOSIS
- DRUG ABUSE
- IMMUNOSUPRESSION
- ASTHMA
- COPD
- CYSTIC FIBROSIS
- OTHERS

1. CHROMOSOMAL ABORMALITIES
2. PREMATURITY

Signature of Candidate **Signature of Supervisor**

FAMILY HISTORY

GENETIC DISORDER:

LABARATORY INVESTIGATION

FREE BETA-hCG

PAPP-A

PlGF

ROUTINE INVESTIGATIONS

Hb

Urine routine

RBS

TSH

HbA2/HPLC

OGTT

USG

NT/NB

CRL

GESTATIONAL AGE

UTERINE ARTERY DOPPLER

ANOMALY SCAN

USG FOR FGR (32-34 WKS)

Signature of Candidate **Signature of Supervisor**

Following tests will be done if needed:

LFT

RFT

SPOT P:C

LDH

URIC ACID

ON FOLLOW UP

All patients:

NEONATAL OUTCOME	**MATERNAL OUTCOME**
BIRTH WEIGHT	MODE OF DELIVERY WITH INDICATION IF CAESAREAN DONE
IF CRIED	GESTATION AT DELIVERY
SEX	GESTATION OF APPEARANCE OF HTN
ABNORMALITIES	GESTATION OF APPEARANCE OF PROTEINURIA
NICU ADMISSION WITH INDICATION	

Patients with abnormal Result:

AMNIOCENTESIS/CVS

FOETAL DNA (ff DNA or NIPT)

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....

.....am willing to participate in the study **"PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"PREDICTIVE VALUE OF FIRST TRIMESTER SCREENING COMBINED WITH PIGF AND UTERINE ARTERY PULSATILITY INDEX FOR PREECLAMPSIA AND ANEUPLOIDY" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____
ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ

_____
ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____

ਪਤਾ _____

ਮਿਤੀ_____

ਪਤਾ _____

_____
ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____
ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ